Antipsychotics Prescribing and Ethnicity

Connolly, Anne Caroline

Awarding institution:
King's College London

Antipsychotic Prescribing and Ethnicity

By

Anne Connolly BPharm, MRPharmS

A thesis submitted for the degree of Doctor of Philosophy to King's College London

Institute of Pharmaceutical Science

Faculty of Life Sciences and Medicine

November 2018

TABLE OF CONTENTS

ABSTRACT

Treatment of mental illness differs between races. Many reports, investigations, public enquiries and surveys have been conducted documenting differences in referral to specialist mental health services, admission rates to hospital, detention under the Mental Health Act and seclusion whilst in hospital. These differences are particularly marked for black patients compared with white.

Concerns about these differences, in addition to research (predominantly from the United States) showing differences in prescribing of antipsychotics for ethnic minorities, have prompted United Kingdom studies investigating any prejudicial prescribing of antipsychotics. Identified differences include use of high doses, more frequent use of older drugs and depot formulations, especially for black compared with white patients. Most of these UK studies were older, had small sample sizes and controlled for few, if any, confounding factors affecting antipsychotic prescribing. A large, multi-centre, cross-sectional survey of antipsychotic prescribing by ethnicity, collecting over 20 potential confounding factors, was undertaken to measure dose, high dose, polypharmacy, type of antipsychotic, cost of antipsychotic, clozapine use and route of administration. The null hypothesis was that black patients receive antipsychotic drug treatment of equal dose, type, number, cost and route to white patients. Data were analysed (using regression methods) for black and white patients alone (as these are the two ethnicities with the most reported differences in medication use), for all ethnicities (to see if any differences for other ethnic groups not only black and white), by individual centre (to determine if prescribing by ethnicity differs by location) and also to determine which factors predicted outcomes. Medical prescriber

attitudes to prescribing by ethnicity were assessed using a case vignette and questionnaire method.

Analysis by ethnicity did not find differences between black and white patients (n=938) in dose (adjusted percentage difference 0.97 [95% confidence interval (CI) -4.28, 6.22], p=0.72); high dose (adjusted odds ratio [AOR] 0.98 [CI 0.63, 1.51], p=0.92); use of first generation antipsychotics (AOR 1.25 [CI 0.87, 1.79], p=0.22); polypharmacy prescribed (AOR 1.15 [CI 0.87, 1.51], p =0.33); polypharmacy administered (AOR 1.08 [CI 0.78, 1.49], p=0.66); or cost of antipsychotic treatment (adjusted effect size 1.75 [CI -9.81, 13.31], p=0.77). Re-analysis including all ethnicities and inclusion of two other outcomes (route of administration and clozapine use), also did not find differences by ethnicity although many variables were associated with the outcomes. Some of these relationships were unexpected, for example the use of lower doses and first generation antipsychotics, but most could be explained rationally.

Analysis of data by the different sites involved revealed differences in prescribing by ethnicity, particularly for one centre. These effects included higher doses, polypharmacy, greater use of 1st generation antipsychotics and higher costs predominantly for black compared with white patients. Unfortunately for some of these outcomes it was not possible to adjust results for potential confounders because of some centres' small sample sizes and missing data.

After dissemination of findings, ethnic minority prescribers reported that they were very surprised with the results of these studies on antipsychotics and ethnicity. They said they purposely prescribed higher doses for black patients as they were more severely ill

on admission to hospital. To test the validity of these comments all medical prescribers at one NHS trust were surveyed using a case vignette and questionnaire. Differences were not found in antipsychotic prescribing by ethnicity for percentage maximum dose (47.7% black, 50.9% white, p=0.57), high dose (1.67% black, 3.33% white, p=0.68), type (1.6% black, 2.5% white, p=0.10), polypharmacy (3.3% black, 6.5% white, p=0.37) and route of administration (intramuscular 0.8% black, 0% white; oral black 44.7%, white 45.5%; oral or intramuscular black 3.3%, white 5.7%; p=0.53) outcomes.

The study was, at the time it was undertaken, the largest UK study of antipsychotic prescribing in black and white patients and the most geographically diverse. Overall clinical and theoretical studies described in this thesis did not show differences in antipsychotic prescribing by ethnicity. Some individual centres may have poorer prescribing by ethnicity that requires remedial action, although such differences were infrequently observed. Nevertheless, for all of these studies significant limitations, including in design and analysis, may have affected these results.

ACKNOWLEDGEMENTS

This thesis would not have been possible without the support and encouragement of my supervisors Professor David Taylor and Professor Graham Davies. I owe them both many thanks. I would also like to express my gratitude to several other professionals who have enabled me to complete this work. They are: Dr Dinesh Bhughra, Dr Victoria Cornelius, Olubanke Dzahini, Peter Milligan, Maria O'Hagan, Anna Sparshatt and John Woodcock. Finally I would like to acknowledge the contributions of all the pharmacists and medical professionals who collected the data for the studies described in this work.

PUBLICATIONS ARISING FROM THIS THESIS

Connolly, A., Rogers, P., and Taylor, D., 2007. Antipsychotic prescribing quality and ethnicity - a study of hospitalized patients in south east London. *Journal of Psychopharmacology*, *21*(2), 191-197.

Connolly, A., and Taylor, D., 2008. Ethnicity and quality of antipsychotic prescribing among in-patients in south London. *The British Journal of Psychiatry*, *193*(2), 161-162.

Connolly, A., 2010. Race and prescribing. *The Psychiatrist*, *34*(5), 169-171.

Connolly, A., Taylor, D., Sparshatt, A. and Cornelius, V., 2011. Antipsychotic prescribing in black and white hospitalised patients. *Journal of Psychopharmacology*, *25*(5), 704-709.

Connolly, A. and Taylor, D., 2014. Factors associated with non evidence-based prescribing of antipsychotics. *Therapeutic advances in psychopharmacology*, *4*(6), 247-256.

Connolly, A. and Taylor, D., 2016. Does race affect prescribing for acute psychosis? Evaluation by a case vignette. *Therapeutic Advances in Psychopharmacology*, *6(3),* 172-177.

LIST OF TABLES

LIST OF FIGURES

List of Appendices

ABBREVIATIONS

ANOVA	Analysis of Variance
BEH	Barnet, Enfield and Haringey
BEN	Benign Ethnic Neutropenia
BME	Black and Minority Ethnic
BNF	British National Formulary
BPRS	Brief Psychiatric Rating Scale
CBT	Cognitive Behaviour Therapy
CGI-S	Clinical Global Impression - Severity
CI	Confidence Interval
CNWL	Central and North West London
CPR	Cardiopulmonary resuscitation
CPZe	Chlorpromazine Equivalence
CYP	Cytochrome p450
DDD	Defined Daily Dose
DRE	Delivering Race Equality
ECT	Electroconvulsive Therapy
ELC	East London and City
EM	Extensive Metaboliser
EU	European Union
FBC	Full Blood Count
FGA	First Generation Antipsychotic
GAF	Global Assessment of Functioning
GAS	Global Assessment Scale
GP	General Practitioner
HAM-D	Hamilton Rating Scale for Depression
HIV	Human Immunodeficiency Virus
IAPT	Improving Access to Psychological Treatments
IM	Intramuscular
MADRAS	Montgomery-Åsberg Depression Rating Scale
MAR	Missing At Random
MCAR	Missing Completely At Random
MHMDS	Mental Health Minimum Data Set
n	Number (of subjects)
NAT	N-acetyltransferases
NEL	North East London
NHS	National Health Service
NIH	National Institutes of Health
NSF-MH	National Service Framework for Mental Health
OR	Odds Ratio
p	Probability
PANSS	Positive and Negative Syndrome Scale
PM	Poor Metaboliser
POMH-UK	Prescribing Observatory for Mental Health – United Kingdom
PRN	When required (pro re nata)
SAPS	Scale for the Assessment of Positive Symptoms
SGA	Second Generation Antipsychotic
SLaM	South London and Maudsley

SMR	Standardised Mortality Ratio
SWLaSG	South West London and St Georges
t-test	Students t-test
TD	Tardive Dyskinesia
UGT	UDP-glucuronyltransferases
UM	Ultra rapid Metaboliser
UK	United Kingdom
US	United States of America
VIF	Variance Inflation Factor
WHO	World Health Organization
YMRS	Young Mania Rating Scale

CHAPTER 1 INTRODUCTION - ETHNICITY AND PRESCRIBING

1.1 RACE AND ETHNICITY

What is race? The Oxford English Dictionary defines race as 'each of the major divisions of humankind, having distinct physical characteristics'. Confusingly it also describes race as 'a group of people sharing the same culture, history, language, etc.; an ethnic group' and has six further definitions. Ethnicity, however, is described as 'the fact or state of belonging to a social group that has a common national or cultural tradition'. In practice the two terms are often used interchangeably, for example when requesting patients' race or ethnic group on hospital admission. As we have seen, neither are simple or precise terms.

Use of the word 'race' has been problematic as it is associated with historical attempts to categorise people by their skin colour and other physical characteristics. These categories have, in the past, been used to defend the use of eugenics and social Darwinism but are a social and political rather than a biological construct. The term 'ethnic group' (United Nations Educational Scientific and Cultural Organiszation, 1950) is sometimes suggested as a preferred term as it includes cultural groups of various kinds and also white people. It is important to use the term 'ethnic group' rather than 'ethnic' as in some cultures, particularly the United States, ethnic is sometimes used to refer to black communities.

When we use the term 'race' we may assume others understand our meaning. Anthropologists study of the term has found that the public say race is based on biological differences, is relatively unchanging and races are easily distinguishable from

each other (MacEachern, 2011). Likewise organisations and Acts of Parliament concerned with equality have traditionally used the term 'race', for example the Commission for Race Equality and the Race Relations Act 2000. These have been renamed respectively as the Equality and Human Rights Commission and repealed for the Equality Act 2010.

How is ethnicity measured in the UK? The largest data collection of ethnicity comes from the UK census. From 1841 census data collected information on country of birth only for persons born outside England and Wales. A question on parents' country of birth was added in 1971 and it was not until the 1991 census that race/ethnicity data were collected in the UK but still not in Northern Ireland (Office for National Statistics, 2006). Respondents were asked about their ethnic group rather than ethnic origin. The categories used then were white, black-African, black-other, Indian, Pakistani, Bangladeshi, Chinese, any other ethnic group. This categorisation was criticised as it did not separate white respondents into any groups and did not allow people to describe themselves as British. By 2001 Northern Ireland was included (white, mixed and Irish Traveller options) and British, Irish, other white and mixed were added. The options then were white (British, Irish, any other white background), mixed (white and black Caribbean, white and black African, white and Asian, any other mixed background), Asian/Asian British (Indian, Pakistani, Bangladeshi, any other Asian background), black/black British (Caribbean, African, any other black background), Chinese or other ethnic groups (Chinese, any other). Furthermore a question on religion was included as for some this is a more important signifier of identity than ethnicity. In the most recent census in 2011 Gypsy/Irish Traveller and Arab were added and Chinese was reclassified to Asian. Categories were as in Appendix 1. The 2011 census also asked a question

about ‘national identity’ allowing respondents to express which country or countries they were most affiliated to (Office for National Statistics, 2011), allowing classification to become more complex and nuanced.

The Office for National Statistics Ethnic Group Classification 2015 recommends using a very similar classification system to the 2011 census (Office for National Statistics, 2015) for data collection. It emphasises the importance of self-identification and allowing respondents to see all possible options available before selection. The UK NHS still uses the 2001 census classification as the national standard for mandatory ethnicity data collection (Department of Health, 2001) so lags behind in its modernity. Scotland recently started using the 2011 classifications.

We can see, over a 20-year period, the subtle changes and increased sophistication of ethnicity classification. Even with these changes critics describe what is being measured as still predominantly race, as opposed to ethnicity. A person’s ethnicity is based as much on subjective factors as the practicalities of place of birth etc. A pragmatic solution has to be reached that incorporates enough variation to allow respondents to feel their ethnicity is accurately described but also allows large enough samples in each group for statistical analysis. Researchers need to be aware of the heterogeneity and limitations of their classifications (Mathur, 2013) as people may be racially similar but culturally distinct. Higher level groupings can mask heterogeneity that is important - for example white groups include the Irish, people from eastern European whilst Asian includes people from Pakistani, Indian, Bangladeshi and since the 2011 census Chinese. These groups can vary in health outcomes because of different socioeconomics and levels of education. For instance, coronary artery bypass graft surgery rates by ethnicity

– worst for Bangladeshi, better for Pakistani and best for Indian people. Grouping these people together as Asian loses these important distinctions. Collapsing ethnic minority groupings risks finding false negative results.

1.2 Ethnicity and Research

1.2.1 Participation in Research

Participation in research studies by minority ethnic groups is crucial so that trial data can be generalised to the populations that are being treated. In addition if the results of research studies are not reported by ethnic group we do not know if treatments are ineffective, intolerable or require adjustment. Inclusion of ethnic groups in research is a core component of ensuring health equality.

National guidelines from the NIH in the US now stipulate that minority ethnic groups must be recruited into clinical trials in adequate numbers (National Institutes of Health, 2001). The NIH Revitalization Act of 1993 (National Institutes of Health, 1993) directed the NIH to produce guidelines to include women and minorities in research, making researchers legally bound to recruit and report data on these groups. This guidance does not specify what proportion of minorities should be included in a study but instead gives advice depending on whether or not previous studies suggest significant or equivocal differences. It also states that when earlier studies suggest there are, or there could be, differences by gender or ethnicity proposals 'must include a description of plans to conduct analyses to detect significant differences in intervention effect by sex/gender, racial/ethnic groups, and relevant subpopulations'.

All clinical trial research in the UK is currently conducted under the EU Clinical Trials Regulation (The European Parliament, 2014). These regulations are a legal requirement

and EU member states must comply with them. Clinical Trials Regulations recently replaced the EU Clinical Trials Directive, but these new regulations do not mandate the recruitment of minority groups into research in the EU as legislation does in the US.

In the UK, as well as EU regulation, the Research Governance Framework for Health and Social Care (Department of Health, 2005b) states in standard 2.2.7 'Research, and those pursuing it, should respect the diversity of human society and conditions and the multicultural nature of society. Whenever relevant, it should take account of age, disability, gender, sexual orientation, race, culture and religion in its design, undertaking, and reporting. The body of research evidence available to policy makers should reflect the diversity of the population.' This does not legally bind researchers, as in the US, nor does it stipulate what proportions of minorities should be included. A new research framework for the UK is currently being updated and is at the consultation stage. It is worth noting that in countries where policies compel ethnic minority participation there is greater reporting of data by ethnicity and inclusion of these groups (Rochon et al., 2004). The UK framework has been described as unsophisticated by merely ensuring minorities are present in samples (Allmark, 2004). Critics suggest that researchers need to identify studies where ethnicity matters (for example where treatment effects differ) and also analyse by ethnicity.

When minorities are included in research studies, in what proportions should they be? A logical suggestion is that the proportions of each ethnic group included in the study mimic that of the population studied. Minorities are included in research so that any differences in treatment can be determined by subgroup analysis. These differences may be in equality of service provision or be used as a proxy for clinical diversity. Reflecting

population proportions does not always ensure adequate numbers for statistical analyses particularly for ethnic groups with smaller representations. This means that larger numbers of patients may need to be recruited at that start of the study and costed for during study planning. Also as race and ethnicity are not biological constructs, including and analysing by race or ethnicity means that we may be unintentionally perpetuating stereotypes as we are assuming that race/ethnicity indicates a specific genetic/disease/clinical characteristic (Rathore & Krumholz, 2003; Smart et al., 2008). This is less important when studying issues such as equality of healthcare provision but can be crucial when attempting to determine biological differences to a treatment.

Studies and reports examining participation of minority groups in research are conflicting (Braunstein et al., 2008; Federal Drugs Administration, 2013; Wendler et al., 2005). The perceived reluctance of minority groups to participate in research is described in several medical specialities including oncology, infectious diseases and cardiology (el-Sadr & Capps, 1992; Federal Drugs Administration, 2013; Murthy et al., 2004; Newman et al., 2006; Ranganathan & Bhopal, 2006; Shavers et al., 2002; Stewart et al., 2007). Most data describes studies from the US with some information from the UK. Other studies, however, report high or as expected rates of participation by proportion of the population (Fisher & Kalbaugh, 2011; Wendler et al., 2005).

Interestingly when examining participation of minorities by phase of clinical trial, representation of black and minority ethnic groups differs. Phase I studies are safety studies in healthy volunteers and phases II and III are in those with the condition needing treatment. Minority groups are overrepresented in phase I studies (Fisher & Kalbaugh, 2011) and the reasons for these differences are unclear. Financial rewards for

exposure to the risks of phase I studies can be an incentive with some people making a career from participation. Some authors have suggested that if minority groups are underrepresented in research this means that the majority population are undertaking disproportionate risks and this is ethnically indefensible. Analysis of participation by phases of research study for ethnic minorities shows this idea to be more complex than a brief examination would suggest.

In order to participate in research minorities need to be invited to take part - willingness is only one aspect of their inclusion. There are many other obstacles to participation; distrust of the medical community; poor access to primary care (minorities are predominantly treated in emergency rooms in the US) with the resultant loss of a consistent relationship with a medical provider; fewer minority health care professionals; not actively recruiting minority participants in places where minorities are geographically located; language difficulties; medical eligibility; prescriber preconceptions of minorities (including perceived reduced intelligence, likelihood of poor adherence to treatment and appointments) and lack of knowledge about clinical trials (Corbie-Smith et al., 2002; Fisher & Kalbaugh, 2011; Shavers et al., 2002; van Ryn & Burke, 2000; Wendler et al., 2005).

The often-cited reason for these concerns is the infamous Tuskegee Syphilis Study. This was a US medical research study, started in 1932, of the natural course of untreated syphilis. The study included approximately 600 black men (numbers quoted vary) - 399 with syphilis and 201 uninfected and continued until 1972 despite effective treatment for syphilis being available in the 1940s. The subjects in the study were assumed to consent by volunteering for the study and were actively deceived by the researchers and

the government into being given treatments known to be inactive. Rigorous efforts were made to keep subjects in the study until after their death so that their condition could be confirmed by post-mortem. The full degree of the systematic deception that occurred has been described in detail (Brandt, 1978) and President Clinton apologised to the survivors of the study and the families of the deceased (Centers for Disease Control and Prevention, 1997). It would be expected that such gross deception and abuse would have a major impact on participation in clinical trials by black people. Some studies support this but there is limited direct evidence (Corbie-Smith, 1999; McCallum et al., 2006). Surveys have found that despite black people being more aware than whites of both the Tuskegee study and the Clinton apology, they are as likely or more likely to participate in research (Brandon et al., 2005; Brown & Topcu, 2003; Katz et al., 2009; Katz et al., 2008). It has also been reported that distrust of the medical and scientific community predates the Tuskegee study and has it origins in the medical experiments conducted on slaves (Gamble, 1997).

Improving minority participation in research can be done by improving access to research opportunities rather than changing mindsets. Trust can be improved in many ways; minorities need to be involved in the planning and management of the study from the start; community and church leaders can promote and recruit subjects; researchers need to develop long-term relationships with the communities from which they are trying to recruit. Practical suggestions also have beneficial effects on recruitment such as informing and inviting minorities though public presentations; providing translators where language barriers exist; offering childcare and travel expenses; recruiting minority researchers whose patients are mostly minorities; involve minority physicians in study design and improving researchers training and experience of working with minority ethnic groups (Swanson & Ward, 1995; Thompson et al., 1996; Wendler et al.,

2005). Participation rates of minorities in phase I clinical trials, where many of these suggestions have been implemented, show they are clearly effective.

1.2.2 Measurement of race and ethnicity in research

An essential component of measuring race and ethnicity in research is that it must be self reported and identified. Race, as discussed earlier, is not anthropologically or genetically derived; it is a social and political construct. As such the National Institutes of Health in the US recommend measuring both race and ethnicity. Ethnicity is measured as Latino/Hispanic or non-Latino/non-Hispanic then race as American Indian or Alaska Native, Asian, black or African American, Native Hawaiian or other Pacific Islander, and white. Each of these ethnic and racial groups are clearly described.

The accurate measurement of race/ethnicity in research is important so that health services are truly equitable and disparity can be investigated. In the past ethnicity was assigned by the interviewer rather than respondent. As ethnicity is a complex concept and can vary by questioner, location and over time, it should be self-assigned. The NHS in England uses the 2001 census classification and the patient is asked 'what is your ethnic group?' then shown a printed list of options to choose from. If this is not possible e.g. for telephone contacts, then a series of questions are asked that guide the respondent through the available categories. The Office for National Statistics produces its own guidance, most recently in 2015, on monitoring of ethnic groups. It also gives advice on merging of categories when they have changed with each census. This is important so that changes over time can be measured against each other.

If we are going to record and analyse information about race and ethnicity then it must be accurate and complete. Recording of ethnicity in the 1990s in NHS primary and

secondary care was poor and it was not until 2006, when financial incentives were introduced, that data collection began to be systematically obtained for newly registered patients in both sectors of the health service. The completeness of ethnic group recording in the NHS since these changes has improved, particularly when primary and secondary care data are combined (Mathur, 2014). Results from studies examining the accuracy of the data collected are conflicting. In one study, where self-recorded ethnicity in hospital records versus a cancer survey was compared, overall ethnicity was correctly recorded in almost 95% of cases but when examined further white ethnicity was broadly correct (over 97%) but for ethnic minorities over 40% of data were found to be incorrect (Saunders et al., 2013). Mathur and colleagues describe highly accurate ethnicity classifications when comparing hospital vs. census data but they examined total data not by ethnic group (Mathur, 2014). Inaccurate recording of ethnicity has also been described in other countries particularly for ethnicities with the smallest proportions in the population. In the US this is more likely if not black or not white (Gomez & Glaser, 2006; Waldo, 2004) whilst in New Zealand, Maori, Pacific groups and Asian ethnicity are poorly recorded (Swan et al., 2006).

1.3 Ethnicity and Health

There is a long history of inequality in provision of health care services to ethnic minorities. There have been many reports and analyses, from the Poor Laws through to the introduction of the welfare state and the NHS, into social inequalities and health. The seminal report into the issue was the infamous Black report in 1980 (Black, 1980). This examined health inequalities and why they had, inexplicably, worsened since the introduction of the NHS. Black showed that the poorest had the greatest risk of ill health and death and that the reasons for this were social inequalities i.e. diet, occupation, education, housing and environment. It was difficult to examine ethnicity and health

inequality at the time as data collection of ethnicity was in its infancy (country of birth was the only measure available) and had not yet been included in censuses. Whilst ethnic minorities were more likely to have a lower occupational class (used as a proxy for wealth and social class in the report) this alone did not explain inequality. Using standardised mortality ratios (SMR = observed deaths/expected deaths x 100) produced some unexpected results. Immigrant workers' SMRs compared favourably with their British-born equivalents. Black suggests that this may be because healthier people are more likely to migrate as they expect to survive and flourish in a new country. But when SMRs for causes of death for ethnic minorities are compared with number of deaths in rank order very different patterns of disease emerge (Senior & Bhopal, 1994). This is because SMRs compare diseases common in the comparison population whereas rank order of deaths emphasises diseases that are common independent of comparison. So it can be seen the importance of measuring ethnicity, ill health and death and that the methods used can have variable results.

Internationally the WHO made an assessment of health inequality in thirteen developed countries (Crombie, 2005). This found that health inequalities existed in all of the countries studied and because poverty and health are interlinked, health and social justice policies should be unified. A WHO target since 1985 has recommended a 25% reduction of inequality between countries and between groups within countries (World Health Organization, 1985).

Since the Black report there have been numerous attempts to measure, analyse and make recommendations to improve health equality. These include the Whitehall I and II studies of staff grade (a proxy for socioeconomic position or social class) and mortality

in the British Civil service (Marmot et al., 1991; Reid et al., 1974). These studies found that, even after controlling for risk factors, the lower the grade of staff the higher the rate of cardiovascular disease. The reasons for this finding are unclear but an increase in stress owing to a lack of control of work, low self-esteem and lower salaries have all been suggested. Unfortunately both these studies of health equality did not collect data on ethnicity. The Black report's recommendations were not accepted or implemented by the government of the time because it had been commissioned and supported by the previous administration and of the financial costs involved. Despite this the report prompted an explosion of research. It was updated by the Heath Research Council (Townsend, 1992), further investigated by the King's Fund (Benzeval, 1995) and eventually a later government (Variations Sub-group of the Chief Medical Officer's Health of the Nation Working Group, 1996). It was not until the 1990s that the issue of health equality was revisited by a public inquiry (Acheson, 1998) and government policy (Department of Health, 1999b). All these reports essentially made the same major argument. Ill health and socioeconomic disadvantage were inextricably related and variations in health services were not the prime reason for variations in health (Marmot, 2001).

The Acheson report (Acheson, 1998) investigated health equality including the effect of ethnicity. He found that for almost all minority ethic groups' mortality ratios were higher than average and that cause of death varied by country of birth. Ethnicity was measured by country of birth on death certificates so only migrant data were analysed, missing many self-identified ethnic minorities born in the UK. For infant mortality only mother's country of birth was recorded on birth certificates at the time making analysis difficult, but mothers from the Caribbean and Pakistan had infant mortality rates about

double the national average. Additionally he described many indications of poorer health for ethic minorities, for example higher rates of limiting long-standing illness for those of Pakistani or Bangladeshi origin than white people. Moreover ethnic minority groups were more likely to live in areas of geographic and economic deprivation that contributed to both between and within ethnic minority group health inequality. In this respect minority groups have more similarities than differences with the majority ethnic group.

Acheson described specific differences in care received by minority groups. For instance use of primary care was similar to the white majority but difficulty in physically accessing their GP, longer waiting times at the surgery, less satisfaction with outcomes and lower referral rates to secondary care were reported. Some of these differences may be because of communication difficulties and lack of cultural competency (i.e. the ability to provide services to patients with different cultural beliefs, attitudes and behaviours and the use of multi-cultural staff in policy development, administration and provision of services). He cites an example of lower rates of cervical screening in South Asian women improved by culturally sensitive explanation of the purpose and procedures of the test.

The Acheson report recommended that ethnic minorities should be present on decision making/advisory panels about health; their needs specifically considered in the development and implementation of policies aimed at reducing socioeconomic inequalities; that data on ethnic minorities needed to improve to monitor inequalities in health. After so many reports and investigations into health inequalities Sir Donald

Acheson wrote in the foreword to the King's Fund report 'today the question is not whether the facts are valid but who cares and what can be done about them'.

More recently the Marmot review of 2010 (Marmot, 2010) was charged with proposing evidence–based strategies for reducing health inequality in England. He once again found that socioeconomic status and worse health outcomes were associated for some but not all ethnic groups.

The 2011 UK census asked two questions about health, one about general health (options; very good, good, fair, bad, very bad) and a second about long-term disability (are your day to day activities limited because of a health problem or disability which has lasted, or is expected to last, at least 12 months? Include problems related to old age. Options; yes limited a little, yes limited a lot or no). These data show us ethnicities with the highest proportions of limiting long-term illness (compared with white) differed by gender and were Pakistani and Bangladeshi women, mixed white-black Caribbean men, white Irish men, black Caribbean men, white Gypsy and Irish Traveller (new category for the 2011 census) men and women and particularly those of older age. Conversely Pakistani, Bangladeshi, Arab and Chinese men had lower rates of limiting long-term illness than whites (Becares, 2013). These effects were not replicated in the question on general health where poorer health was reported. Better rates of limiting long-term illness were reported for other white, black African and Chinese.

Geographically London had the most severe health inequalities by ethnicity in England and Wales. We can see that the results are complex and differences occur by ethnic group with gender (see Figure 1 and 2 below, age-standardised ratios of limiting long-term illness for ethnic minority groups compared to white British by gender).

FIGURE 1 ETHNIC INEQUALITIES LIMITING LONG-TERM ILLNESS FOR MEN 2011

From http://www.ethnicity.ac.uk/medialibrary/briefingsupdated/which-ethnic-groups-have-the-poorest-health.pdf

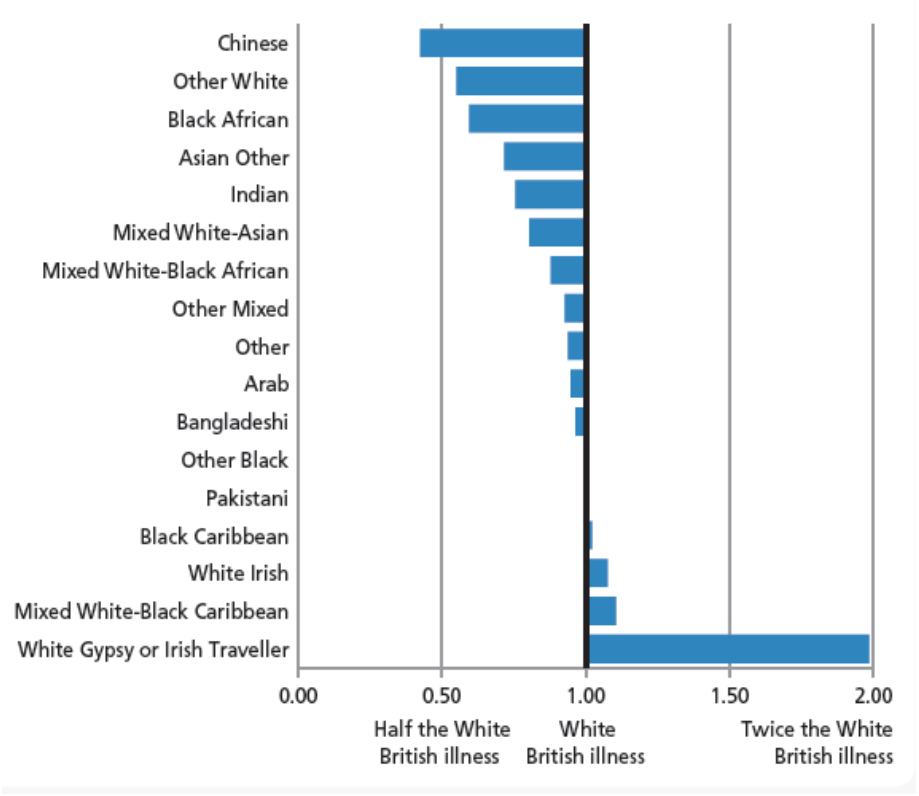
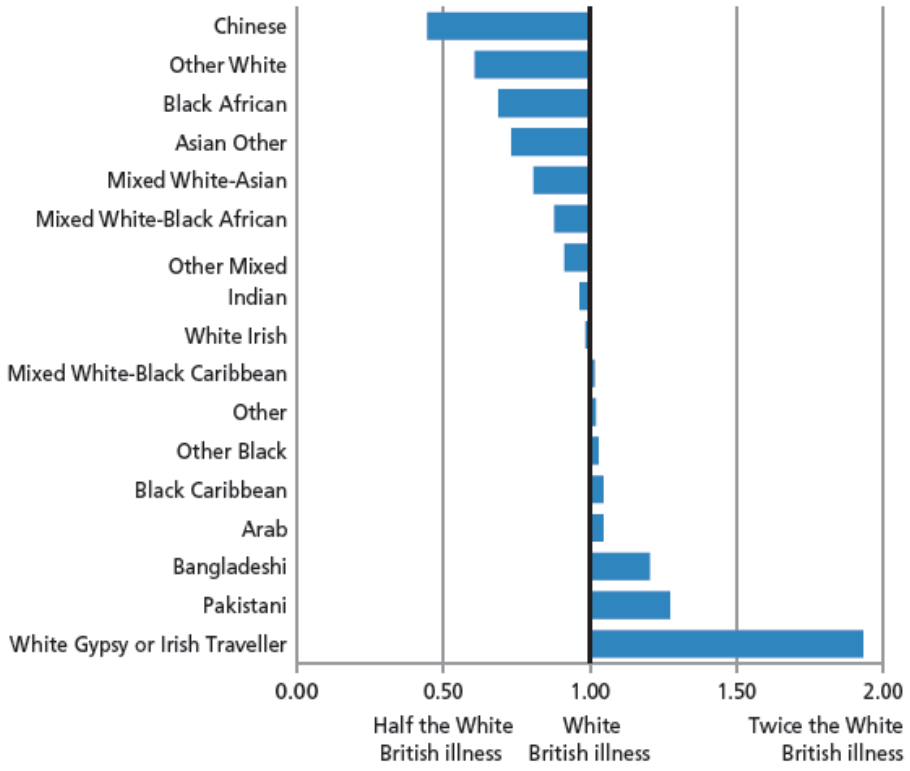


FIGURE 2 ETHNIC INEQUALITIES LIMITING LONG-TERM ILLNESS FOR WOMEN 2011

From http://www.ethnicity.ac.uk/medialibrary/briefingsupdated/which-ethnic-groups-have-the-poorest-health.pdf



Measurement of ethnicity data allows us to determine if any inequalities exist between ethnic minorities and the majority population. The importance of collecting these data has been strengthened most recently by the Equality Act 2010 which legally ensures that public bodies must provide equitable health services. The NHS must publish data to show that they are adhering to the legislation and, if not, has to show what steps are to be taken to achieve equality of provision.

We can see that significant health inequality occurs within minority ethnic groups and between them and the majority population. This difference is not wholly explained by lower socioeconomic status in minorities.

1.3.1 Ethnicity and Physical Health

Specific differences in the provision of health services to minority ethnic groups have been consistently found across a wide range of medical disciplines. US studies of treatment by ethnicity highlight many areas of poorer quality health services. African Americans are less likely than the majority to receive optimal cardiac medication; coronary artery bypass surgery; cancer testing, treatments and pain relief; stroke care; rehabilitation and nursing home services (Ball & Elixhauser, 1996; Goel et al., 2003; Johnston et al., 2001; Sander et al., 2009). They are also more likely to receive some surgical procedures such as orchidectomy (Bjurlin et al., 2012) and amputations (Feinglass et al., 2005). This is even after controlling for factors such as health insurance, age, symptoms, disease severity, under/over use of services and patient income. These differences are, unsurprisingly, associated with higher mortality rates for African Americans.

Perceptions of treatment and the reality of care are at odds with each other. Surveys in the US show people think that ethnic minorities do not receive different treatment from the white majority (Lillie-Blanton et al., 2000). The reasons for these differences are partly but not completely explained by poverty and poorer access to care as there are other factors that may be contributing such as discrimination and stereotyping. Suggested solutions include increasing proportions of ethnic minorities among health care professionals, improving access to speciality care, allowing appeals for denials of care, enforcing equality rights legislation, promoting use of evidence-based guidelines, using interpreters to enhance communication and financial incentives to enhance choice of provider.

In the UK we would perhaps expect healthcare to be different. The NHS is a government-funded equitable healthcare system where treatment is given on the basis of need and not ability to pay. It has a well-developed primary care and public health system, unlike in the US, which aids prevention, detection and treatment of disease earlier. Nevertheless there are still health inequalities by ethnicity. Specifically these include lower rates of cervical cancer screening and coronary angioplasty for minorities (particularly South Asian populations (Feder et al., 2002; Webb et al., 2004)) and significantly higher rates of infant mortality in Caribbean and Pakistani communities (Gray et al., 2009). Rates of certain health conditions also differ by ethnicity in the UK. Mortality ratios for lung cancer are higher for Scottish and Irish groups but lower for black African, black Caribbean and South Asians; Bangladeshi and Pakistani people have higher rates of coronary artery disease; South Asians and Caribbean people are more likely to have type 2 diabetes; lifestyle differences in fruit and vegetable intake, physical activity, smoking, alcohol use and obesity rates are worse for some but not all minority groups in the UK (Aspinall & Jacobson, 2004).

1.3.2 Ethnicity and Mental Health

1.3.2.1 Recent History

Treatment of mental illness in minority ethnic groups differs from the majority (Department of Health, 2003; 2005a). There have been many reports, investigations and recommendations detailing large differences in referral, admission, seclusion and detention rates for different ethnicities – particularly when data from black and white patients are compared.

Modernisation and reform of mental health services was planned through the National Service Framework for Mental Health for adults (Department of Health, 1999a). This described evidence-based national standards, their aims, development, delivery and performance measurement. Research on ethnicity and mental health was examined as part of their process and reported:

- In black compared with white patients - higher rates of psychotic illness, referral to mental health services through the criminal justice system rather than GPs or social services, admission to hospital under the Mental Health Act, treatment with physical rather than psychological therapies and admission to secure services. (Davies et al., 1996; Koffman et al., 1997; McKenzie et al., 1995; Nazroo, 1998)
- Depression diagnosed less frequently in Asian people compared with white despite higher rates of suicide in Asian women (NHS Centre for Reviews and Dissemination, 1996).
- Stigma because of mental illness worsened by racism, ethnicity affects access to treatment (Commander et al., 1997).
- Mental health assessments are often not sensitive to ethnicity (McKenzie et al., 1995). Staff need skills in cultural competence and the NHS must attract and retain staff from BME communities.
- Ethnicity monitoring not satisfactory in the NHS and needed to improve.

Unfortunately the NSF-MH, despite reporting these differences by ethnicity, did not set standards for mental health services specifically for minority ethnic groups.

After the NSF-MH in 1999 an amendment was made to the Race Relations Act in 2000 that forced all public bodies, including the NHS, to eliminate racism in public services. Two reports, ‘Breaking the Circles of Fear’ (Keating et al., 2002) and ‘Inside Outside’

(Department of Health, 2003), were produced as result of this change. 'Breaking the Circles of Fear' was a qualitative study that examined the relationship between mental health services and African and Caribbean communities. Key themes were the sources (perceptions, attitudes, diagnosis, hospital experiences) and consequences (limited trust and engagement, delays in seeking help) of fear of mental health services. The study concluded that these fears affect access to services resulting in delays in treatment and coercive care.

'Inside Outside' examined the inequalities in provision of mental health services for ethnic minorities and set targets to reduce and eliminate these differences and improve services. The report stated that ethnic minorities were more likely to experience institutional and coercive care, that individual patients needs were not given priority and that institutional racism existed in mental health care. It described the evidence for disparities in mental health care for ethnic minorities by using the seven national standards and five key areas i.e. health promotion (including discrimination and social exclusion), primary care and access to care, effective services, carers and suicide of the NSF-MH. These standards and the reports findings are outlined below:

Standard 1: Mental Health Promotion. Health and social services should provide mental health for all, combat discrimination and promote social inclusion.

- Racism and stigma affect psychiatric morbidity.
- Individuals from black and minority groups are at
    - greater risk of developing mental health problems than the majority.
    - increased risk of hospital admission and coercive care (especially African Caribbean and Irish people).
    - elevated risk of suicide (especially for the Irish and South Asian women).

- greater risk of readmission (especially for black patients).

Standard 2: Primary Care. Patients who contact primary care with a mental health problem should have this identified, assessed, treated and, where necessary, referred to specialist care.

- Research suggests GPs may be less likely to recognise psychiatric disorder in ethnic minority patients.
- Consultation rates for anxiety and depression may be reduced for some groups (especially for South Asians and the Chinese) but increased in others (the Irish).
- Language and cultural barriers affect assessment.
- Recognition of mental health problems (particularly for black and South Asian patients) and referral to specialist services is affected by ethnicity.
- Lack of involvement of patients' GPs associated with compulsory admission and police involvement.

Standard 3: Access to Services: individuals with a mental health problem should be able to make contact with local services 24 hours a day.

- There are barriers to ethnic minority groups successfully accessing services and they are less satisfied with these services after contact.
- Cultural stereotyping may affect access to services e.g. Irish people stereotyped as having alcohol problems prevents treatment for mental illness.
- Ethnic minorities are likely to access care through coercion, compulsory admission and the involvement of the criminal justice system.

Standard 4 and 5: Effective services for people with severe mental illness. Patients with severe mental illness should receive the treatment and services they need. Crises should be prevented where possible and if they do occur treated quickly and efficiently in a hospital bed near home. Ethnic minorities

- are more likely than the majority population to be misdiagnosed, prescribed drugs and ECT and less likely to be referred for psychotherapy.
- have higher readmission rates, longer hospital stays and are less likely to have their social and psychological needs addressed.
- rights and health care needs are taken less seriously than for white patients on acute psychiatric units.
- are more likely to be assessed as needing medium and high secure psychiatric care and, particularly for African Caribbean people, are overrepresented in forensic services.
- are less satisfied with mental health services but are more satisfied with newer treatment services such as home treatment, crisis resolution and early intervention but, for African Caribbean patients, not intensive case management.

Standard 6: Caring about carers: health and social services must assess the needs of and provide care for carers of people receiving specialist mental health services. There is little research available about carers' experience of mental health services for ethnic minorities. Concerns reported through surveys and stakeholder events:

- Carers of black patients feel unable to make treatment decisions and find community services and they are also concerned about doses of antipsychotic medication.
- Carers want information about mental illness and how best to support relatives and

also want to be listened to and involved in care decisions.

- Advocates that are culturally appropriate are needed.

Standard 7: Preventing Suicide. Health and social care services aim to achieve the target of a reduction of national suicide rate by one fifth by 2010 (Saving Lives: Our Healthier Nation (Department of Health, 1999b)).

- Suicide by ethnicity is not recorded at inquests or on death certificates (this is still the case now as death certificates record place of birth only).
- Women of South Asian and East African origin and Irish people have higher suicide rates than those born in England and Wales.

After documenting these mental health inequalities by ethnicity the report describes changes needed both inside services and outside within communities. The objectives and changes were as follows:

i. To reduce and eliminate ethnic inequality in mental health service experience and outcome by consulting with mental health agencies and stakeholders in the community and ensuring accountability and change through clinical governance (i.e. standards of care).

ii. To develop a culturally capable service i.e. ethnic minorities should receive the same treatment as the majority through: developing a diverse and culturally sensitive workforce; ensuring the voluntary sector works with the NHS to develop services for minority groups; mental health services that are flexible and adaptable to working with different cultures; improving access to translation services for people.

iii. To set national standards to improve access, care experience and outcome. They

proposed to do this by: collection of ethnicity data; training GPs in cultural awareness; assessing patients mental state in their own language; auditing referrals to specialist mental health services and psychotropic drug use annually; reducing coercive care by access to crisis teams, crisis care plans and audit of Mental Health Act use by ethnicity; mental health assessments should be carried out with family/carers and interpreter or advocate; care plans to include cultural, religious or spiritual beliefs; ensuring families and carers have information on legal, advocacy, second opinion rights; ensuring NHS trusts have an Equality Framework for audits.

iv. To enhance the cultural relevance of research and development by developing research methods for use in minority ethnic groups and including these groups in all research.

In the same year as the 'Inside Outside' report there was a public inquiry into the death of David Bennett (Norfolk Suffolk & Cambridgeshire Strategic Health Authority, 2003). David Bennett was a black patient who died of positional asphyxia during a restraint at a medium secure mental health unit in Norfolk in 1998. This was not the first time a public inquiry into the death of a black patient in a mental health unit had been undertaken. In 1993 there had been a public inquiry (Prins, 1993) into the deaths of three black patients at Broadmoor hospital, namely Michael Martin in 1984, Joseph Watts in 1988 and Orville Blackwood in 1991. All three patients died after being restrained and given injections of antipsychotic drugs. The report described how black people were more likely to be brought into hospital by police; detained under the Mental Health Act; kept on locked wards; be transferred from prison to secure units; receive medication and less likely to receive psychotherapy. The recommendations of

the report were to introduce training in the management of violent incidents without restraint; monitor and research diagnosis of Afro-Caribbean patients; training for staff in resuscitation; black appointee to advise on race awareness and equal opportunities and development of a procedure for informing relatives of the death of a patient.

At around the same time as the Orville Blackwood inquiry, the Ritchie inquiry (Ritchie, 1994) investigated the care and treatment of Christopher Clunis, a black patient who stabbed and killed a man on the London Underground in 1992. Christopher had schizophrenia, was unwell at the time of the attack and not taking medication. The inquiry found that the many services that were involved in his care (mental health services, the police, primary care, social services, the Crown Prosecution Service) did not communicate and share information with each other and so his risk of violence was not properly recognised. Lack of resources meant that he was not managed by a forensic service and his medication was not reviewed. He was treated with depot antipsychotics and, on one admission, very large doses of antipsychotic medication (chlorpromazine 2000mg regularly plus up to 1600mg when required daily). The inquiry examined the effect of ethnicity on Christopher's treatment and found that there was no discrimination or prejudice against him. But they did report that staff were too willing to accept that he misused street drugs and diagnose him with drug-induced psychosis. In reality he did not misuse street drugs but had schizophrenia. The report comments also on the overrepresentation of black patients with schizophrenia in mental health services and detained under the Mental Health Act.

The inquiry into the death of David Bennett, five years later, described in detail the circumstances leading up to, during and after his death. He had been restrained by

several nurses (between three and five - testimonies were confused) in the face down or prone position for somewhere between 15 and 25 minutes. On the night of his death he had taken his oral regular medication as usual and was not administered any medication during the restraint. David was taking large doses of several medications concurrently i.e. clozapine 700mg, haloperidol 40mg, sulpiride 200mg and valproate 200mg (to prevent seizures). The total percentage maximum dose (i.e. calculating each dose as a proportion of the BNF maximum dose and then multiplying by 100), using the doses that were licensed at that time, was approximately 106%. If current maximum doses were used this would be 286%. This is because the maximum dose of haloperidol was 200mg and has been repeatedly reduced to the current maximum oral dose of 20mg. The pathologist did not consider that David's medication was the cause of his death and his post-mortem blood results were normal (but levels of medication in a body after death are notoriously difficult to interpret (Taylor et al., 2015)). But David was receiving high dose antipsychotic polypharmacy, as had Orville Blackwood before him (fluphenazine decanoate 150mg IM single dose with promazine injection 150mg given to manage violent behaviour: 125% percentage maximum dose). Using high doses and more than one antipsychotic confers an increased risk of a range of side effects including movement, anticholinergic, metabolic, seizures, sedation, neuroleptic malignant syndrome, QT prolongation, arrhythmia and sudden cardiac death.

Other failings in David Bennett's treatment included the lack of availability of a doctor on site (it took 1½ hours for a doctor to get to the unit) and that his family were not notified of his death until the next morning. Many of the 22 recommendations of the David Bennett enquiry had been previously made by the Orville Blackwood enquiry. Recommendations included training in cultural awareness, control and restraint, CPR

and first aid; assessment of ethnic minorities mental state; acknowledgement by the government of institutional racism in mental health services; appointment of a National Director of Mental Health and Ethnicity; policy for racist abuse in mental health services; care plans to detail ethnicity and cultural needs; workforce should be ethnically diverse; restraints in the prone position should be for a maximum of 3 minutes; collection of data on deaths of psychiatric inpatients by ethnicity and use of control and restraint; research into the management of treatment-resistant schizophrenia; access to second opinion in mental health for all patients; detention in secure hospital only when necessary; review of financial assistance for patients leaving hospital; movement of patients between hospitals justified in writing; families of deceased psychiatric patients to be given care and support; medication in mental health to be used within maximum doses. The need to translate good intentions and recommendations into actions was highlighted.

Controversially the David Bennett inquiry reported, as had 'Inside Outside' (Department of Health, 2003) and 'Delivering Race Equality in Mental Health Care' (Department of Health, 2005a), that mental health services were institutionally racist. The term was original described in the Macpherson report (Macpherson, 1999) into the Metropolitan police handling of the death of Stephen Lawrence, a black teenager who was stabbed to death in a racially motivated attack in 1993. He said "Institutional racism is the collective failure of an organisation to provide an appropriate and professional service to people because of their colour, culture, or ethnic origin. It can be seen or detected in processes, health systems, attitudes and behaviour which amount to discrimination through unwitting prejudice, ignorance, thoughtlessness and racist stereotyping, which disadvantage minority ethnic people". Some commentators state

institutional racism is about systems and policies that affect outcomes for minority groups rather than direct racism (McKenzie & Bhui, 2007) but this has been vociferously disputed (Singh, 2007). Other researchers have also described mental health services as institutionally racist, quoting higher rates of admission and involuntary admissions and longer stays as evidence. They argue that while incidence rates may be higher for black people it is prevalence that is reflected in hospital admission data (McKenzie & Bhui, 2007) and community prevalence rates do not differ by ethnicity (Nazroo, 1997). These views have been rejected by some (Fearon & Murray, 2007) contending that community prevalence studies using the same data report high rates of hallucinations (Johns et al., 2002) and psychotic symptoms (King et al., 2005) in ethnic minorities. Others report higher admission rates are because of higher rates of psychosis in black patients (Singh & Burns, 2006). They argue that rates of psychosis are higher in all immigrant groups globally including for Western minorities and that detention rates are higher because fewer referrals for black patients come from GPs and more from the police. This was because families of black patients are more likely to contact the police rather than medical services when a member of their family is ill for the first time and argue that this does not reflect institutional racism, as there has been no prior contact with mental health services. They attribute the difference in method of referral to the stigma of mental illness in these communities, with behavioural problems requiring legal rather than medical help (Singh & Burns, 2006). Differences in involuntary admission rates they explain are because of referral through the courts or police (Murray & Fearon, 2007), presentation to services without a family member in attendance (carers seek help earlier), living alone, higher rates of unemployment, low levels of social support, growing up in the inner city, being separated from a parent or suffering physical abuse in childhood and racist experiences -

all factors that are more likely for black, and particularly for black Caribbean, patients. They argue that accusations of institutional racism damage research into the reasons for these marked differences for black people and those working in mental health services do not operate in isolation - education, employment, housing, social services and the criminal justice system all combine to affect risk of admission (McKenzie & Bhui, 2007). Others contend that under and delayed treatment of patients is where the problem lies and that suggestions of a need for separate services for minority ethnic groups are themselves racist and a form of psychiatric apartheid (Murray & Fearon, 2007; Singh, 2007). There is also concern that those who deny mental health services are institutionally racist and that they too will be deemed racists (Murray & Fearon, 2007). Confusingly the UK government accepted direct and indirect discrimination by ethnicity did occur (Department of Health, 2005a), but now the Department of Health says that the NHS is not institutionally racist (Murray & Fearon, 2007).

The government's response to the Bennett inquiry and accusations of institutional racism were the introduction of the NHS Race Equality Action plan (listing actions and those responsible for health services, outcomes and developing people) and the publication of Delivering Race Equality in mental health care, an action plan for reform inside and outside services (Department of Health, 2005a). The DRE report planned more appropriate and responsive services (action to develop organisations and the workforce), community engagement (engage communities through 500 new Community Development Workers) and better information (improved monitoring of ethnicity, better dissemination of information and good practice, census of mental health patients). The plan was for a service for ethnic minorities of less fear and increased satisfaction; reduced rates of admission to hospital; reductions in violence and

seclusion; prevention of deaths after physical intervention; better states of recovery; greater access to talking treatments; more active role in training of professionals; development of policy; a culturally competent workforce. Ultimately it should deliver equality of access, experience and outcome for ethnic minorities. The government accepted the recommendations of the Bennett inquiry in DRE with some minor variations - stating the prone position of restraint should be used as a last resort rather than it should be used for a maximum of 3 minutes and that services should not be discriminatory rather than saying services are institutionally racist. One of the major recommendations was that an annual census be undertaken of inpatients in mental health and learning disability services.

The Count Me In Censuses of mental health and learning disabilities services (Care Quality Commission, 2010) began in 2005 and continued until 2010. They were designed to collect accurate data on the ethnicity of users and enable health services to achieve the goals of DRE by tracking progress using this data. Overall there was little change in the 6 years in admission and detention of ethnic minorities. This may not be surprising given that 31% of patients had been in hospital for more than a year (the censuses overrepresent long-stay admission and underrepresent short-stay admissions). In 2010 the census collected information on 32,799 inpatients in 261 NHS and independent healthcare organisations in England and Wales or outpatients under a community treatment order. The key findings are as described in Table 1. Differences in rates refer to statistically significant differences from national rates.

TABLE 1 KEY FINDINGS, COUNT ME IN CENSUS 2010 (CARE QUALITY COMMISSION, 2010)

Number of patients	32,799 (including 2,959 outpatients on a CTO), of whom 23% were from Black and minority ethnic groups (that is, not White British)
Distribution of patients	16% of all patients were in independent hospitals. 70% of patients from Black and minority ethnic groups were at 25 of the 261 organisations involved
Rates of admission (excluding outpatients on a CTO)	Lower than average for the White British, Indian and Chinese groups In line with the average for the Pakistani and Bangladeshi groups Higher than average for the other minority ethnic groups (particularly for the Black Caribbean, Black African, Other Black, White/Black Caribbean Mixed and White/Black African Mixed groups, who had rates two to six times higher than average)
Referral from the criminal justice system	Higher than average rates for some Black and White/Black groups
Detention under the Mental Health Act on admission*	Higher than average rates for the Black Caribbean, Black African, Other Black and White/Black Caribbean Mixed groups, White Irish, Other White and Other Mixed groups
Detention under section 37/41	Higher than average rates for the Black Caribbean and Other Black groups
Community treatment order	Higher than average rates for the South Asian and Black groups
Seclusion	Higher than average rates for the White/Black Caribbean Mixed, White/Black African Mixed, Black Caribbean and Black African groups
Self-harm	Higher than average rates for the White British group Lower than average rates for the Black and South Asian groups
Accidents	Higher than average rates for the White British group Lower than average rates for the Black groups
Hands-on restraint and physical assault	Few ethnic differences were apparent
Length of stay (from admission to census day)	31% of patients had been in hospital for one year or more; 20% for more than two years Length of stay longest for patients from the Black Caribbean and White/Black Caribbean Mixed groups; shortest for patients from the Chinese and Bangladeshi groups
Single sex accommodation	61% of men and 77% of women not in a designated single sex ward; 13% of men/16% of women without access to designated single sex toilet and bathing facilities; 37% of men/39% of women without access to a designated single sex lounge area/day space (these proportions generally lower among minority ethnic groups) (see page 27 for definition of single sex accommodation)

* Excluding outpatients on a CTO. Rates for the different ethnic groups for overall applications of the Mental Health Act, including CTOs, showed broadly similar patterns to detention rates on admission day that excluded patients on a CTO. In both cases, rates were higher than average among the Black Caribbean, Black African, Other Black and White/Black Caribbean Mixed groups.

For learning disability services the main differences were in rates of admission – lower for other white, Indian, Pakistani, other Asian, black African, Chinese and other groups and two to threefold higher for white and black Caribbean, mixed, black Caribbean, other black and other mixed groups. Other notable differences were that two thirds of patients had been in hospital for one year or more and almost a third for five years.

Changes over the 6 years were few for mental health:

- Overall number of inpatients fell by 12%.
- Proportion in independent hospitals rose from 10 to 16% i.e. by 60% or 6 percentage points.
- Proportion of patients from minority ethnic groups increased from 20 to 23% i.e. by 15% or 3 percentage points (population of ethnic minorities also rose by 8% from 2005 to 2007).
- Admission rates remained similar:
    - Lower than average for white British, Indian and Chinese groups.
    - Average for Pakistani and Bangladeshi groups.
    - Higher than average for black and white/black mixed (more than two times average), other black 'exceptionally high rate of admissions'.
- Rates of referral from GPs and community mental health teams were lower in black and white and black groups, referral from the criminal justice system was higher.
- Increase in number of patients detained under the Mental Health Act (40% in 2005, 49% in 2012).
- Rates of self-harm lower among black and South Asian groups.
- Few differences in hands-on restraint, physical assault, accidents.

DRE goals for minority ethnic groups were:

- A decline in admission rates – two or more times higher for black and white/black mixed, six times higher for other black groups, lower for Indian, Chinese.
- To reduce detention rates - higher in all six censuses for black Caribbean, black

African, other black, almost consistently higher for black and white Caribbean and other white groups. Higher than average detention under section 37/41 (criminal courts use section 37 to refer patients to hospital instead of prison, section 41 allows a court to place restrictions on discharge (this order added if risk to public as Ministry of Justice as well as psychiatrist control admission)) for black Caribbean and other black groups.

- To reduce seclusion - higher for black and white, black mixed groups and other white groups in three of the six censuses.

The next step after 'Count me in' was to move on from counting patients in hospital to understanding the factors that result in variations in rates and routes of admission to hospital for ethnic minorities. The Care Quality Commission recommended that mental health services worked with other statutory agencies including police, the criminal justice system, voluntary groups and minority communities to prevent and intervene earlier in mental ill health. They emphasised the importance of good quality data collection after these censuses. The data are collated for both hospital and community mental health services by the NHS Information Centre in the Mental Health Minimum Data Set and so provides a larger sample size and more detailed information as most patients (more than 90%) are located in the community.

A review of DRE (Melba, 2010) found that the sheer number of recommendations (78 in total) made it difficult for organisations to focus on them all. Progress was made in many areas but lack of organisational understanding of what was required, variable data collection and quality meant that, for some recommendations, outcomes were difficult to assess.

The government's new strategy for mental health, after DRE, was No Health without Mental Health (Department of Health, 2011). This aimed to reduce the socioeconomic risks of mental ill health, reduce inequalities and improve outcomes – very similar aims to DRE. Key objectives included 'parity of esteem' of mental to physical health and integration of mental and physical health services. The report mentions, once again, equality and fairness and highlights the need to collect data on suicide, differences in rates of mental illness, admission and detention rates of minority ethnic groups.

Recent data from 2015 for mental health and learning disability analysed from MHMDS has still found major differences for some ethnic minorities (Health and Social Care Information Centre, 2015).

- 'The black or black British group had the highest proportion of people who had spent time in hospital in the year, which meant that 12.7 people per 100 who were in contact with mental health and learning disability services from this ethnic group spent at least one night in hospital in the year. This is higher than the figure for any of the other ethnic groups and more than double the figure for the white ethnic group.'
- 'People from the black or black British ethnic group were more likely than other ethnic groups to be detained, with 56.9 detentions per 100 inpatients.'
- 'The black or black British ethnic group had the highest percentage of people who were cared for under Care Programme Approach (a national system which sets out how mental health and learning disability services should help people with mental illnesses and complex needs) in the year at 37.2%, which is much higher than the number for all ethnic groups.'

Analysis suggested these figures could be related to greater or more complex needs once in contact with services for these ethnic groups.

We have seen through numerous reports and inquiries that inequalities exist in mental health services. The risk factors and potential causes of these differences are complex but may be related to diagnosis, pathways to care and different rates of mental illness in some ethnic groups.

1.3.2.2 DIAGNOSIS AND RATES OF PSYCHOSIS AND SCHIZOPHRENIA IN ETHNIC MINORITIES

Rates of psychosis and schizophrenia are much higher for black patients in the UK than white (Bhugra et al., 1997; King et al., 1994; Van et al., 1996). What are the reasons for these differences and are they to do with racism by mental health services or are other factors important?

There have been concerns that ethnic minorities, particularly black patients, are more likely than whites to be diagnosed with schizophrenia (Neighbors et al., 1989; Sashidharan, 1993; Sashidharan & Francis, 1999; Schwartz & Blankenship, 2014). These differences have occurred even after using standardised diagnostic criteria and interview (Neighbors et al., 1989) and have been suggested to include clinician bias owing to cultural stereotyping and Eurocentric diagnostic practice (Mukherjee et al., 1983; Singh & Burns, 2006), under-diagnosis of depression and bipolar disorder (Barnes, 2008), language difficulties (Department of Health, 2003), ethnic differences in presentation (Mukherjee et al., 1983) and clinicians' own ethnicity (Trierweiler et al., 2006).

Other research studies examining diagnosis have repudiated these causes. A case vignette diagnosis and treatment study, in which only one detail (ethnicity) varied, found British psychiatrists, regardless of which country they were trained, were less likely to diagnose schizophrenia in black patients compared with white (Lewis et al., 1990). In addition a study comparing the diagnoses of a Jamaican and a British psychiatrist for UK patients found they diagnosed a similar proportion with schizophrenia but disagreed as to exactly which patients had the condition (Hickling et al., 1999). Diagnosis in black people may also be affected and confused by differing symptoms that UK psychiatrists recognise as schizophrenia, for example hallucinations may be more frequent and culturally more acceptable in non-Western countries (Johns et al., 2002). Black people may also have a different illness course with more relapse, remission and social disturbance but fewer negative and persistent symptoms (Sharpley et al., 2001).

The incidence of schizophrenia has been found to be similar in people in the West Indies as in the UK (Sharpley et al., 2001) but much higher for black people in the UK (Kirkbride et al., 2006), particularly for the siblings of black second-generation patients with schizophrenia. This indicates that environmental factors are affecting risk and vulnerability (Hutchinson et al., 1996).

Some social risk factors disproportionately affect the black community such as being the child of a single parent, separation from parents, and being brought up in the care system. Cannabis is a risk factor for psychosis particularly when use is heavy and with a high potency product (Di Forti et al., 2015; Marconi et al., 2016). Data are contradictory about whether use is similar in black and white patients – reportedly the same in those with psychosis but lesser for black immigrants than white native populations (Cantwell

et al., 1999; Sharpley et al., 2001; Veen et al., 2002). However other more recent studies suggest use is greater in black populations (UK Drug Policy Commission, 2010). Urban environments are stressful and black people are more likely to live in inner cities where social isolation, living in areas with a low population of your ethnic origin, overcrowded housing, overstimulation, crime, pollution and living alone can be more common (Bhugra & Bhui, 2001).

Ways of accessing mental health services i.e. 'pathways to care' can help us understand further why rates of hospital admission are higher for minority groups. Black patients are more likely to be referred to services by police, less likely to be referred by GPs, and more likely to be admitted compulsorily. What causes these differences? Delays in help-seeking results in use of emergency services, stereotypes of black men as more dangerous and violent, unemployment, living alone, residing in social housing are all risk factors for compulsory admission (Pipe et al., 1991).

Severity of psychosis has been reported to be worse for some ethnicities e.g. Chinese and South Asian patients in Canada (Chiu et al., 2016), African Americans in the US (Arnold et al., 2004). But other studies have found no such differences (Connolly & Taylor, 2008; Kim et al., 2014) and, in the UK, have instead focussed on measuring diagnostic incidence, inpatient admission and detention rates as indirect measures of illness severity (Kirkbride et al., 2006; Mann et al., 2014).

Black and white patients and relatives have similar rates of satisfaction with mental health services but black patients are more likely to see services as racist, and specifically second-generation black patients, are less satisfied than older first-generation blacks and whites. Interestingly the greater the number of previous admissions the more likely patients are to be less satisfied, indicating that dissatisfaction

develops over time and may be a factor delaying seeking help from mental health services (Parkman et al., 1997).

Can racism against ethnic minorities cause mental illness? Studies in the US have found that minor daily discrimination can lead to ill health and that unfulfilled aspirations and obstruction of opportunity cause psychological stress. Moreover the psychological effects of racism include external attributions of negative events (owing to a negative view of self) resulting in paranoia and delusions (Sharpley et al., 2001). The impact of racism on the development of psychosis is unknown but some studies have found an association between the two (Janssen et al., 2003; Karlsen et al., 2005).

A key question is why are these social factors associated with psychosis but not depression and anxiety? Possible explanations include reduced help-seeking behaviour in ethnic minorities; GPs failing to notice psychiatric symptoms because of patients' somatic presentation to avoid the stigma of mental illness; avoidance of the effects of racism being defined as anxiety or depression. Nevertheless studies show similar or greater prevalence of depression and anxiety in black compared with white people. So why is psychosis not so markedly elevated in South Asian populations? Acculturation is a stressful experience and so living an insular life with ones own community may be protective. Rates of unemployment are lower in South Asian populations than black so improved socioeconomic status and upward mobility may be protective factors.

Could migration be a factor? The seminal study by Ødegaard (Ødegaard, 1932) found that Norwegian immigrants to the US were more likely to develop schizophrenia than Americans born in the US or native Norwegians. He hypothesised that people who migrate are themselves at greater risk of schizophrenia but later studies showed this to be incorrect as it would not explain the higher risk for second-generation migrants

(Cantor-Graae et al., 2003; Selten et al., 2002). Other studies in the UK, Denmark and the Netherlands have found similar results to Ødegaard (Cantor-Graae et al., 2003; Cantor-Graae & Selten, 2005; Selten et al., 2001). Results are not uniform for all migrants. For instance Turkish migrants to the Netherlands, unlike other migrant groups, do not have an elevated risk of schizophrenia (Selten et al., 2001). A systematic review and meta-analysis of migration and schizophrenia found a relative risk of 2.7 (95% CI 2.3, 3.2) for first-generation migrants and 4.5 (95% CI 1.5, 13.1) for second-generation migrants (Cantor-Graae & Selten, 2005). Risks were greater for those migrating from developing vs. developed countries and from areas where the majority population is black (vs. white or not black or white). The reasons for this are unclear but were suggested to be an increased risk of schizophrenia in the country of origin and environmental risk factors in Western society. When the incidence of schizophrenia was studied both in the WHO ten-country study (Jablensky et al., 1992) (Colombia, Czechoslovakia, Denmark, India, Ireland, Japan, Nigeria, the USSR, the UK, and the US) and in a separate study in Barbados (Mahy et al., 1999) no significant differences by country were found. It is worth noting that black men are one group that are less likely to be counted in UK national censuses and some authors have suggested this may affect incidence calculations by as much as 10-30%. So raised incidence in country of origin and in people who choose to migrate are unlikely to be causes of increased rates of schizophrenia. This suggests risks are environmental, for example living in an urban environment and the degree of this urbanicity. Research is still some way behind in explaining these differences adequately.

In summary, higher rates of diagnosis of schizophrenia and admission to mental health units for ethnic minorities have complex social and environmental not genetic causes.

What is clear is that the reasons for these differences have not been fully elucidated and further hypotheses and testing are required to provide an explanation.

1.3.2.3 ETHNICITY AND PSYCHOLOGICAL TREATMENT

There are concerns that access to psychological treatments for ethnic minorities are poor. Commitments made to monitor and improve the situation are stated in DRE and the government's Improving Access to Psychological Treatments programme (Department of Health, 2005a; 2009). Even after the introduction of IAPT, Asian, black and other groups are underrepresented in initial assessment statistics for psychological therapy. These differences represent low referral rates to these services (Glover et al., 2010). As well as poor access, ethnic minorities are less likely to receive psychotherapy, particularly black vs. white patients (OR 0.33, 95% CI 0.16, 0.71) (Department of Health, 2003; Mays, 1985; McKenzie et al., 2001).

Studies of CBT for schizophrenia show that black patients have higher dropout rates and poorer outcomes (Rathod et al., 2005). Various reasons have been proposed for these differences including: difficulty in engagement; cultural stereotyping as 'not psychologically minded'; attitudes of professionals; and lack of understanding of other cultures (Rathod et al., 2005). The reasons for termination of psychotherapy include a negative attitude towards the therapist and lack of belief in effectiveness of treatment. Cultural adaptation of CBT for minority groups could improve these results (Rathod et al., 2010).

Having psychology professionals that represent the minority ethnic groups they serve is an important factor in enhancing trust and acceptance of psychological therapies (Department of Health, 2009). Matching client and therapist by ethnicity may improve

numbers of completed sessions and reduce drop-out rates (Flaskerud & Liu, 1991). Data are difficult to locate on the proportion of psychology professionals by ethnicity in the UK, but examining access to postgraduate clinical psychology courses can serve as a proxy measure. In 2016 17% of those accepted to a place on these courses were from an ethnic minority (University of Leeds, 2015). This compares with 14% of the UK population being from an ethnic minority in the 2011 census, thus indicating a diverse population of trainees. Examining membership of the British Society of Psychologists in 2016 reveals, of members who declared ethnicity, only a tiny proportion were non-white i.e.1.7% were black and 6.7% other (British Psychological Society, 2016). Thus the diversity of psychologists in the UK does not reflect the UK population. This has important cultural implications as people from ethnic minorities may wish to see a therapist with a similar cultural and linguistic background to themselves.

Access to and receipt of psychological treatment by ethnicity are important issues to monitor but so to is acceptance of treatment after it has been offered. There are concerns that some black patients may be more likely to refuse the offer of CBT treatment. Trust in services, the stigma of mental illness and therapist ethnicity are important factors affecting ethnic minorities acceptance of psychological therapies (Gary, 2005; Shea & Yeh, 2008; Thompson & Alexander, 2006).

1.3.2.4 ETHNICITY AND METABOLISM OF PSYCHOTROPIC MEDICATION

Most psychotropics are not excreted unchanged in the urine – they have to be metabolised by the body to make them more polar and less lipid soluble so they can be removed by the kidney. This metabolism occurs in several organs but most takes place in the liver which contains pockets of enzymes called microsomes. Drug metabolism occurs in two stages to make drugs more polar and usually inactive. Phase I is when

oxidation, reduction or hydrolysis occurs and phase II joins drugs or their metabolites to another substance for example through glucuronidation, acetylation, sulfation, methylation and glutathione conjugation (Preston, 2015).

Liver microsomes contain an enzyme system called cytochrome P450, a family of enzymes that oxidise many psychotropics. The CYP450 enzymes were evolved in animals over billions of years to detoxify plant poisons and consist of over forty different isoenzymes. Only eight of these isoenzymes are responsible for 90% of the metabolism of commonly used drugs. These are CYP3A4, CYP2D6, CYP2C9, CYP1A2, CYP2C8, CYP2C19 and to a lesser extent CYP2B6 and CYP2E1. There are a few other enzymes involved in phase I reactions e.g. functional monoamine oxidases. Phase II conjugation reaction enzymes are less well understood with glucuronidation by UDP-glucuronyltransferases the subject of much research. Drugs may be removed by and induce or inhibit transporter proteins such as the efflux pump P-glycoprotein. This may affect absorption, distribution and elimination of medication and cause drug interactions.

Genetic variation can affect the metabolism of psychotropics as some of the CYP450 enzymes are subject to 'genetic polymorphism', i.e. some people may have variants of these isoenzymes with different activity. People may be poor metabolisers, intermediate metabolisers, normal metabolisers (confusingly described as extensive metabolisers) or ultra rapid metabolisers. A person's metabolising status is genetically determined and can vary by ethnic group.

The CYP450 enzymes that metabolise antipsychotics are predominantly CYP1A2, CYP2D6 and CYP3A4 (Preston, 2015; Taylor et al., 2015). Details are in Table 2.

TABLE 2 CYTOCHROME P450 ENZYMES METABOLISING ANTIPSYCHOTICS

CYP450 Enzyme	**Substrates**		**Inhibitors**		**Inducers**
	Major	***Minor/unknown effect***	***Major***	***Unknown/unclear effect***	***Major***
CYP1A2	Asenapine Clozapine Olanzapine	Chlorpromazine Fluphenazine Haloperidol Perphenazine Pimozide Trifluoperazine	None	Fluphenazine Perphenazine	None
CYP2D6	Aripiprazole Olanzapine Perphenazine Risperidone Zuclopentixol	Chlorpromazine Clozapine Fluphenazine Haloperidol Pimozide Quetiapine	Asenapine	Chlorpromazine Clozapine Fluphenazine Haloperidol Levomepromazine Perphenazine Risperidone	None
CYP3A4	Aripiprazole Lurasidone Pimozide Quetiapine	Chlorpromazine Clozapine Haloperidol Perphenazine Risperidone	None	Perphenazine Pimozide	Asenapine

Ethnic differences in CYP450 activity have been identified for all three of the major enzymes that metabolise antipsychotics i.e. CYP1A2, CYP2D6 and CYP3A4 (McGraw & Waller, 2012). This means that some populations may metabolise psychotropics more slowly or quickly than others resulting in higher or lower plasma levels of these drugs.

Determining the effects of genetic polymorphism on CYP450 enzymes is difficult. Ethnicity, as discussed earlier, is in itself challenging to classify and can erroneously combine people in a category who are very different. This means that inter-ethnic as well as between ethnic differences in metabolising capacity can be marked. The increasing movement of peoples means ethnic isolation has been replaced by ethnic diversity making genotypes less predictable.

CYP1A2 is active mostly in the liver and accounts for approximately 15% of the activity of CYP450 enzymatic hepatic system (Wynn et al., 2008). Environmental factors are also important as smoking and some foods (e.g. cruciferous vegetables, charcoal grilled foods) can also induce CYP1A2. PMs of CYP1A2 are 5% of Australians, 14% of Japanese, 5% of Chinese with lower activity also reported for South and East Asian and African populations compared with Caucasians (Perera et al., 2012; Relling et al., 1992; Yang et al., 2012; Zhou et al., 2009). The activity of CYP1A2 has clinically significant effects on the elimination of olanzapine and clozapine (Murray, 2006).

CYP2D6 is probably the best studied of the CYP450 enzymes to be investigated for its effects on drug interactions. It is a low-capacity, high-affinity enzyme i.e. will metabolise drugs in low concentrations but if concentrations rise then CYP3A4 or

CYP1A2 (high capacity, low affinity enzymes) will clear the drug. This means CYP2D6 PM status may be compensated for by other enzymes (Wynn et al., 2008). CYP2D6 is found in the brain, prostate, bone marrow and heart as well as in relatively small amounts in the liver (2-4% of CYP450 total liver content).

CYP2D6 is polymorphic. PMs of CYP2D6 number approximately 1% in South and East Asians, 5-10% in whites and 0-19% in blacks (Bernard et al., 2006; McGraw & Waller, 2012). Interethnic variation can be pronounced e.g. black PM of CYP2D6 comprise 1.8% of Ethiopians compared with 19% of black South Africans (Bernard et al., 2006). Ultra-extensive and intermediate metabolisers also exist and proportions of these do vary by ethnicity, for instance 60% of East Asian people are intermediate metabolisers of CYP2D6 whilst 21% of Saudi Arabians and 29% of Ethiopians are UM (Bernard et al., 2006; Wynn et al., 2008).

CYP3A4 accounts for 30% of CYP450 activity in the liver and 70% in the small intestine. It is a high-capacity, low-affinity enzyme so where there are low concentrations of a drug metabolised by CYP3A4 other CYP450 enzymes may be active. If CYP3A4 is inhibited it may be difficult for the other low-capacity, high-affinity enzymes to cope with metabolism so drug levels can rise. There are many polymorphisms of CYP3A4 but their effect on metabolic activity is as yet unknown and there is high inter-individual variability in activity between the different isoforms (Hsieh et al., 2001; McGraw & Waller, 2012; Wandel et al., 2000). CY3A4 polymorphisms are associated with several diseases including breast and prostate cancers, secondary leukaemias, diabetes and hyperlipidaemia (Zhou et al., 2006).

So overall whilst one would expect that genetic polymorphism of CYP450 enzymes would have an important effect on dosing of psychotropics for Asians (antipsychotic dose reductions of 20% have been suggested in expert opinion surveys for East Asian people (Gardner et al., 2010)) it would not explain differences in prescribing between other ethnic groups. That is not to say that metabolising ability has no effect on dosing or adverse effects of medication (indeed PM of CYP2D6 have a greater risk of developing tardive dyskinesia and extrapyramidal side effects) but that an individual's own metabolising ability may be more important than their ethnicity alone (Wynn et al., 2008). Currently in the UK determining CYP450 polymorphisms is prohibitively expensive through laboratory genotyping or response to a probe (substance metabolised by the CYP450 enzyme in question e.g. for CYP1A2 caffeine, CYP2D6 dextromethorphan, CYP3A4 midazolam) and is usually only possible within a clinical trial. Technological developments mean there are now commercially available tests e.g. the AmpliChip that can quickly and easily detect metaboliser status for CYP2D6 and CYP2C19. In time the UK may be able to test all patients routinely, as is done in some other countries (Mrazek, 2010).

Of course CYP450 metabolism is not the only method of drug metabolism. Acetylation by N-acetyltransferases is a phase II conjugation reaction and is subject to genetic polymorphism and ethnic difference. Some individuals are slow acetylators and can experience greater toxicity with some drugs e.g. hydralazine, isoniazid, procainamide and sulfasalazine but not as yet for antipsychotics (Ackenheil & Weber, 2004; Preston, 2015). Other methods of drug interaction possibly affecting antipsychotics are drug transporter proteins which carry drugs across biological membranes. The most studied is P-glycoprotein, an efflux pump that pushes drugs out of cells and is subject to genetic

polymorphism. It can be induced or inhibited by drugs but is mostly important for metabolism of cancer and HIV drugs and is not thought to affect or transport antipsychotics (Preston, 2015). It is worth noting that P-glycoprotein and CYP3A4 operate in a coordinated way. In the intestine P-glycoprotein increases the time a drug is exposed to CYP3A4 reducing bioavailability whilst the reverse occurs in the liver. The interplay between the two systems is under research. Other drug transporters also exist but their effects on antipsychotics are not known.

1.3.2.5 ETHNICITY AND ANTIDEPRESSANT TREATMENT

Data on the prevalence of depression in ethnic minorities are conflicting. Some authors have found that depression is more common in certain ethnic minorities whilst others have found the opposite (Acheson, 1998; Riolo et al., 2005; Sprotson K, 2002; Williams et al., 2007). This may be because these people with depression are less likely to access care and treatment, resulting in a more severe and chronic condition (Alegria et al., 2008; Williams et al., 2007).

Antidepressant treatment may vary by ethnicity. Black and Asian patients (but not Hispanic (Sleath et al., 2001)), especially those living in areas of high ethnic density, are less likely than whites to be prescribed an antidepressant (Alegria et al., 2008; Gonzalez et al., 2008; Walters et al., 2008). Even in vascular disease, where depression is associated with higher mortality, rates of antidepressant use are much lower in black compared with white patients even after adjustment for depression severity (Waldman et al., 2009). Conversely a study of psychiatrists' assessments of video vignettes of late life depression that differed by gender and ethnicity (African American or white) found no differences in diagnosis or treatment (Kales et al., 2005). This suggests that factors other than ethnic bias are also important. Racial differences in acceptability of use of

antidepressants have been cited as a potential cause of these findings (Cooper et al., 2003) with ethnic minorities preferring counselling and prayer as treatments for depression (Givens et al., 2007a). However antidepressant stigma appears to be greater in white compared with black patients (Givens et al., 2007b).

When ethnic minority groups do take antidepressants there appear to be few differences in the speed of response and remission rates compared with the majority population (Lesser et al., 2007; Lesser et al., 2010) as long as an effective dose is prescribed (Cornwell & Hull, 1998). This is despite polymorphic differences in serotonin and noradrenaline transporters genes, which can differ by ethnicity, affecting antidepressant response (Kim et al., 2006).

1.3.2.6 ETHNICITY AND ANTIPSYCHOTIC TREATMENT

Are there differences in prescribing of psychotropics in minority ethnic groups that relate to prejudice rather than metabolism? Patients and carers think so (Department of Health, 2003; South London and Maudsley NHS Trust, 2005) and, after the inquiry into the death of David Bennett (Norfolk Suffolk & Cambridgeshire Strategic Health Authority, 2003), the issue needed investigation (Department of Health, 2005a).

Most of the studies examining psychotropic use by ethnicity have been completed in the US. Differences in antipsychotic treatment by ethnicity include; an increased likelihood of receiving an antipsychotic (Delbello et al., 2000; Flaskerud & Hu, 1992; Szarek & Goethe, 2003) (refuted by a meta-analysis (Puyat et al., 2013)), higher doses (Diaz & De Leon, 2002; Segal et al., 1996; Walkup et al., 2000), older drugs (Daumit et al., 2003; Fleck et al., 2002) and more frequent use of depot formulations (Kuno &

Rothbard, 2002). Again these differences are pronounced for black compared with white patients. These studies analysed mostly large US databases and adjusted for only a few confounding factors affecting the prescribing of antipsychotics (see Appendix 2 for list of studies and confounders). The healthcare systems of the UK and US differ markedly and have a profound effect on access to and receipt of treatment. Many of the US studies did not adjust for health insurance status.

There are few UK studies examining ethnicity and antipsychotic use. One survey (Lloyd & Moodley, 1992) found no significant differences (after adjustment for five confounding variables) in overall doses of antipsychotics taken by black and white patients, but black patients were more likely than whites to be receiving a depot and at a significantly higher dose. My cross-sectional surveys of antipsychotic prescribing and ethnicity have included large numbers of patients from three NHS trusts and accounted for multiple confounding factors (Connolly et al., 2007; Connolly & Taylor, 2008). Overall these surveys found did not find significant differences between black and white patients for antipsychotic dose, high dose (>100% of maximum dose) or type prescribed (FGA or SGA), even after adjustment for over 20 different confounding factors. But both higher costs of antipsychotic medication and polypharmacy (more than one antipsychotic prescribed) were significantly more likely in black patients (Connolly & Taylor, 2008).

A detailed literature review of antipsychotic prescribing by ethnicity is described in Appendix 3 and summarised in Appendix 4. The outcomes from Appendix 4 are summarised in Table 3 below. Overall there are, broadly, a larger number of prescribing studies that show worse outcomes for black patients (vs. white or non-black or

Hispanic), non-white (vs. white), Hispanic (vs. white or non-Hispanic) and Maori (vs. non-Maori) patients. However studies of Asian ethnicities have mostly better (or similar) outcomes than other ethnicities, although the number of studies are few.

TABLE 3 ANTIPSYCHOTIC PRESCRIBING AND ETHNICITY STUDIES - NUMERICAL SUMMARY OF STUDY OUTCOMES

Ethnic comparison	Outcome	Results (number of studies)			
		Worse	No difference	Better	Total
Black vs. white (reference)	Antipsychotic use	9	11	5	25
	Antipsychotic prescribed	0	1	0	1
	Antipsychotic administered	0	0	1	1
	Dose	8	18	4	30
	High dose	4	8	0	12
	Polypharmacy	6	10	2	18
	PRN antipsychotics	0	1	0	1
	Depot use	11	3	0	14
	Route	0	1	0	1
	Type of antipsychotic (FGA)	3	1	0	4
	Type of antipsychotic (SGA)	14	10	0	24
	Oral SGA	1	0	0	1
	Oral FGA	1	0	0	1
	Depot SGA	0	0	1	1
	Depot FGA	1	0	0	1
	Clozapine use	7	0	0	7
	Clozapine cessation	0	1	0	1
	Cost	1	1	1	3
	Length of treatment	1	1	0	2
	Anticholinergic agent use	1	0	0	1
	‘Off label’ SGA use	0	0	1	1
	Stimulant and SGA use	1	0	0	1
	Service user choice of antipsychotic	0	1	0	1
	Written information provided	0	1	0	1

	Benefits/side effects explained	0	1	0	1
	Total	***69***	***70***	***15***	***154***
Ethnic comparison	**Outcome**	**Results (number of studies)**			
		Worse	**No difference**	**Better**	**Total**
Black vs. non-black (reference)	Antipsychotic use	1	2	0	3
	Dose	2	2	0	4
	Depot use	5	0	0	5
	Type (FGA)	2	1	0	3
	Type (SGA)	4	2	1	7
	Clozapine use	1	0	0	1
	Polypharmacy	0	1	0	1
	Anticholinergic agent use	1	0	0	1
	Antipsychotic injection number of doses	1	0	0	1
	Low dose (< 300mg CPZe)	1	0	0	1
	Stimulant and SGA use	0	1	0	1
	Antipsychotic plasma levels	1	0	0	1
	Total	***19***	***9***	***1***	***29***

Ethnic comparison	Outcome	Results (number of studies)			
		Worse	**No difference**	**Better**	**Total**
White vs. non-white (reference)	Antipsychotic use	2	6	4	12
	Dose	0	3	1	4
	High dose	0	0	3	3
	Depot use	0	3	3	6
	Length of treatment	0	1	0	1
	Anticholinergic agent use	0	0	1	1
	Clozapine use	0	3	1	4
	Low dose (< 300mg CPZe)	1	0	0	1
	Type (FGA)	0	1	1	2
	Type (SGA)	0	8	4	12
	Polypharmacy	1	4	1	6
	Cost	1	0	0	1
	'Off-label' SGA use	0	0	1	1
	Antipsychotic indication	0	1	0	1
	Total	***5***	***30***	***20***	***55***

Ethnic comparison	Outcome	Results (number of studies)			
		Worse	**No difference**	**Better**	**Total**
Asian vs. white (reference)	Antipsychotic use	0	2	2	3
	Dose	0	2	5	7
	Polypharmacy	1	3	0	3
	Type of antipsychotic	0	1	0	1
	High dose	0	1	0	1
	Depot use	0	1	0	1
	Clozapine use	0	1	0	1
	Service user choice of antipsychotic	0	1	0	1
	Written information provided	0	1	0	1
	Benefits/side effects explained	0	1	0	1
	Anticholinergic agent use	0	1	0	1
	Switching from FGA to SGA	0	1	0	1
	Total	***1***	***14***	***7***	***22***
Asian vs. black (reference)	Dose	0	2	1	3
	Polypharmacy	0	2	0	2
	Total	***0***	***4***	***1***	***5***
Asian vs. Hispanic (reference)	Dose	0	2	1	3
	Anticholinergic agent use	0	1	0	1
	Total	***0***	***3***	***1***	***4***
Asian vs. non-Asian (reference)	Dose	0	0	2	2
	Anticholinergic agent use	1	0	0	1
	Total	***1***	***0***	***2***	***3***

Ethnic comparison	Outcome	Results (number of studies)			
		Worse	**No difference**	**Better**	**Total**
Mixed vs. white (reference category)	Antipsychotic use	0	1	0	1
	Type of antipsychotic	0	1	0	1
	Depot use	0	1	0	1
	Clozapine use	0	1	0	1
	High dose	1	0	0	1
	Polypharmacy	0	1	0	1
	Service user choice of antipsychotic	0	1	0	1
	Written information provided	0	1	0	1
	Benefits/side effects explained	0	1	0	1
	Total	**1**	**8**	**0**	**9**
Chinese/other vs. white (reference category)	Antipsychotic use	0	1	0	1
	Type of antipsychotic	0	1	0	1
	Depot use	0	1	0	1
	Clozapine use	0	1	0	1
	High dose	0	1	0	1
	Polypharmacy	0	1	0	1
	Service user choice of antipsychotic	0	1	0	1
	Written information provided	0	1	0	1
	Benefits/side effects explained	0	1	0	1
	Total	**0**	**9**	**0**	**9**

Ethnic comparison	Outcome	Results (number of studies)			
		Worse	**No difference**	**Better**	**Total**
Hispanic vs. white (reference)	Antipsychotic use	2	3	2	7
	Dose	2	5	3	10
	High dose	0	1	0	1
	Polypharmacy	0	5	1	6
	Type (SGA)	5	2	0	7
	Type (FGA)	0	1	0	1
	Clozapine use	4	0	0	4
	Depot use	0	1	0	1
	Cost	0	0	1	1
	Anticholinergic agent use	0	1	0	1
	'Off-label' SGA use	0	0	1	1
	Total	***13***	***19***	***8***	***40***
Hispanic vs. black (reference)	Dose	1	1	1	3
	Polypharmacy	0	0	2	2
	Type (SGA)	0	0	1	1
	Total	***1***	***1***	***4***	***6***
Hispanic vs. non-Hispanic (reference)	Antipsychotic use	0	1	0	1
	Dose	0	1	1	2
	Polypharmacy	1	0	1	2
	Type (SGA)	3	0	0	3
	Total	***4***	***2***	***2***	***8***

Ethnic comparison	Outcome	Results (number of studies)			
		Worse	**No difference**	**Better**	**Total**
Mexican American vs. white (reference)	Type (SGA)	1	2	0	3
	Total	***1***	***2***	***0***	***3***
American Indian vs. white (reference)	Antipsychotic use	0	1	1	2
	Total	***0***	***1***	***1***	***2***
Maori vs. non-Maori (reference)	Antipsychotic dose (CPZe)	0	1	0	1
	Depot use (FGA)	1	1	0	2
	Type (SGA)	1	1	0	2
	Clozapine use	0	0	1	1
	Total	***2***	***3***	***1***	***6***
Asian, Maori and Pacific Islanders vs. non-ethnic minority (reference)	Antipsychotic use	0	1	0	1
	Total	***0***	***1***	***0***	***1***
Hawaiian or multiracial vs. white	Antipsychotic use	0	0	1	1
	Total	***0***	***0***	***1***	***1***

1.4 RATIONALE FOR RESEARCH

There have been calls from reports into mental health services and ethnicity for annual audits of psychotropic drug use (particularly antipsychotics) and ethnicity (Department of Health, 2003; 2005a). This is to establish if there are any differences in prescribing (i.e. dose, route, type, number, cost) by ethnicity. There are inequalities in mental health care and, from my extensive review in Appendices 3 and 4, evidence of differences in prescribing by ethnicity. Such differences require investigation.

The Department of Health's 'Delivering Race Equality in Mental Health Care: An action plan for reform inside and outside services' (Department of Health, 2005a) and the Government's response to the Independent inquiry into the death of David Bennett (Norfolk Suffolk & Cambridgeshire Strategic Health Authority, 2003) in 2005 state;

- 'Organisations should have information capable of being analysed by ethnicity on factors such as medication. If an organisation finds, for example, that average doses of antipsychotic medications are higher for African-Caribbean men, or that novel antipsychotic prescribing is lower, it should investigate why. If there is no clinical reason for the variation, then the organisation should act to reduce it.'
- 'Commissioners and service providers should consider whether it would help local service development to monitor ethnicity in relation to specific aspects of treatment and care, for example using different categories of medication – novel antipsychotics, high dose prescribing etc.'

The undertaking of larger pharmacoepidemiological (e.g. computer database) studies is precluded by the need to collect data on, and correct for, numerous potential confounders of prescribing practice (although the effects of overadjustment need to be considered).

This extent of data collection is best undertaken in inpatient units where data can be readily and accurately recorded. In the present study the aim was to examine the influence of ethnicity on antipsychotic prescribing practice in inpatient units serving populations with the largest proportions of black and minority ethnic group people in the UK.

This thesis will investigate differences in prescribing practices according to ethnic origin while attempting to account for influences of other variables. Mental Health trusts provide services to a wide range of service users from diverse ethnic backgrounds. Results should inform us of any need to investigate further the reasons for any differential prescribing practices.

1.4.1 Hypothesis

The null hypothesis is that black patients receive antipsychotic drug treatment is equal to white patients.

1.4.2 Aim

The purpose of the study is to discover if non-white patients receive different doses (dose, high dose) or treatment (type, number, cost) of antipsychotics compared with white patients.

1.4.3 Objectives

- To describe antipsychotic prescribing by ethnicity.
- To collect multiple confounding factors that may be affecting the outcomes.
- To compare prescribing by black and white ethnicity to determine if ethnicity influences any of the outcomes (i.e. dose, high dose, type of antipsychotic, polypharmacy, cost of antipsychotic).

- To analyse the data for each centre involved in the study by black and white ethnicity to determine if individual centres affect prescribing.
- To analyse the data for other minority ethnicities to determine the relationship with outcomes.
- To determine which clinical variables predict study outcomes.
- To investigate the effect of 'when required' dosing on polypharmacy rates.
- To investigate the effect of prescriber attitudes to prescribing by ethnicity.

1.4.4 STUDIES CONTAINED IN THIS THESIS

- Study 1, Chapter 2 - cross-sectional survey of antipsychotic prescribing (i.e. dose, high dose, type of antipsychotic, polypharmacy, cost of antipsychotic) by black and white ethnicity. This study will investigate prescribing of antipsychotics in black and white patients and collect variables that may be affecting the outcomes to establish if there are any differences in prescribing of antipsychotics by these ethnicities. It fulfils calls from reports into ethnicity and mental health services to investigate prescribing practices in the UK because of differences found in research studies (see Table 3). Most studies and concerns about prescribing have been in black compared with white patients. These are the two ethnic groups with the largest proportions of inpatients in UK NHS mental health trusts so this analysis was done first.
- Study 2, Chapter 3 - analysis of antipsychotic prescribing by black and white ethnicity for each centre involved in the study. This study analyses data for black and white patients for each individual centre alone and then all data combined with centre included as a variable. Study 2 builds on study 1 by investigating variation in prescribing practice between NHS Trusts for black and white patients not just within these ethnic groups.

- Study 3, Chapter 4 - predictors of antipsychotic prescribing for all ethnicities. This study investigates prescribing of antipsychotics for people of all ethnicities not just black and white patients. It builds on study 2 by investigating a larger sample, including proportionally smaller ethnic groupings, to discover if prescribing varies by these ethnicities.
- Study 4, Chapter 5 - case vignette questionnaire study analysing prescribers attitudes to antipsychotic prescribing by ethnicity. This study of theoretical prescribing intention for a black or white patient investigates prescribing by ethnicity using a different method to those used in studies 1, 2 and 3. It builds on these earlier studies by exploring antipsychotic prescribing by ethnicity with a different research design.

CHAPTER 2 ANTIPSYCHOTIC PRESCRIBING BY BLACK AND WHITE ETHNICITY

2.1 GENERAL INTRODUCTION

People of black and minority ethnic groups are overrepresented in mental health services in the UK compared with their white counterparts (Department of Health, 2005a). There are many suggested reasons for this including: delays in seeking help from mental health services; routes of access to these services (Bhui et al., 2003); differences in diagnosis (e.g. overdiagnosis of black people with schizophrenia) (Barnes, 2004); exposure to risk factors for mental illness (e.g. substance misuse) and institutional racism in mental health services (Kirkbride et al., 2006; McKenzie & Bhui, 2007).

Antipsychotic prescribing varies by ethnicity in many countries and has been studied particularly in the US. As discussed extensively in the introduction to this thesis, there are numerous studies examining the pharmacokinetic, pharmacodynamic and prescribing of psychotropics in people of different ethnicities (see Appendices 3 and 4). A small proportion of antipsychotic prescribing variability may be explained by pharmacokinetic differences for some ethnicities, for example differences in metabolism by Asian people (Oesterheld, 2009). This programme of work examines antipsychotic prescribing specifically rather than other aspects of biological variability in order to test the effect of patient ethnicity, rather than inter-ethnic pharmacokinetic and pharmacodynamic differences, on prescriber decisions.

As well as research studies finding differences in prescribing of antipsychotics by ethnicity, reports and investigations into ethnicity and mental health in the UK have also recommended analysis. Most concern is reported for differences in prescribing for black compared with white patients. This is because these are the two ethnic groups are the largest proportions of inpatients in mental health hospitals and black patients are an overrepresented group. This study addresses these concerns by measuring antipsychotic prescribing by ethnicity for black and white patients.

2.1.1 Background

Antipsychotic prescribing by ethnicity had been previously studied firstly in my own NHS trust, the South London and Maudsley, and then in neighbouring trusts, South West London and Saint George's and Oxleas. A cross-sectional survey method was used and data collected using a data collection form, from patient interviews, case-notes and prescription charts. These two initial studies were important development steps in the design and analysis of the third multicentre study. Without these preliminary studies there would not have been an understanding, with the benefit of hindsight and peer review, of the strengths and limitations of the study methods.

Ethnicity is only one of many influences affecting how antipsychotics are prescribed, so the study design needed to collect a range of factors to control for these variables, and allow any differences in prescribing because of ethnicity alone to be statistically isolated.

The initial data collection form was developed using three methods. Firstly a list of all the possible factors that could affect prescribing of antipsychotics was devised. This

was undertaken following the completion of a literature review (using Medline, Embase and Google Scholar citation databases) of antipsychotic prescribing by ethnicity. The research studies identified were examined for variables that had been collected by previous researchers and this information was collated into a table (Appendix 2). This enabled previous work to be replicated and to further develop the area of study through collection of additional factors affecting prescribing of antipsychotics by ethnicity. Lastly expert opinion was sought from clinical colleagues to determine the relevance and appropriateness of these factors to allow review and refinement.
Information from these methods was then examined to determine if data could be feasibly collected on these factors. Finally all the information was collated and incorporated into an antipsychotics and ethnicity data collection form number 1 (Appendix 5).

The peer review process of publication during the first antipsychotic prescribing and ethnicity study highlighted limitations with the data collection. Data on severity of illness was not collected, a factor which could obviously affect prescribing of antipsychotics. This variable was included in the data collection form (Appendix 7) and notes (Appendix 8) for the second study of SLaM, SWLaSG and Oxleas prescribing by ethnicity (Appendix 9) (Connolly & Taylor, 2008).

The first study collected data on patients who had taken an antipsychotic for 3 weeks or longer. This was to exclude periods of dose titration or switching of medication. On reflection it was realised that data should be collected for all patients prescribed an antipsychotic, regardless of treatment length. This was because high doses could have

been used on initiation of treatment for different ethnicities and that excluding these patients could be missing important data.

Patients were interviewed individually for the two initial studies for several reasons. They were asked their own ethnicity, parental ethnicity, smoking status, educational level, employment status, first language, if they had been given a choice of antipsychotic treatment and if the pros and cons of their antipsychotic treatment had been explained.

Ethnicity is usually self-ascribed (Office for National Statistics, 2003) however the study tested prescribers perception of a patient's ethnicity at the point of prescribing of an antipsychotic, rather than the individual's preferred description. This meant self-ascription of ethnicity was not essential. Initially parental ethnicity was collected to determine if patients were black or white or of mixed ethnicity. It was realised that this again was inaccurate as ethnicity is derived over many generations and does not only result from parental ethnicity. Mixed ethnicity patients were not included in these two initial studies. This was for two reasons. Firstly collection of data for only black or white patients would make results clearer and secondly black and white ethnicities were the largest inpatient groups. In this study data were collected on all ethnicities including mixed so that a full examination of prescribing in each group could be undertaken (see Chapter 4 for all ethnicities analysis).

Again the peer review process of the second study made suggestions for improvement of data collection. As the study was cross-sectional in design, collection of the severity of illness measure occurred on the day of data collection, not on the date of starting an

antipsychotic. This rendered this data unrepresentative, as it was often some time since the antipsychotic had been started or the dose increased. Because of this the severity of illness factor was not collected for this final study.

Both initial studies allowed greater testing of the modified data collection form and important insights into how to improve the methods. The final data collection form is in Appendix 12 and accompanying notes for data collection are in Appendices 10 and 11.

2.1.2 Funding

Our initial study (Connolly et al., 2007) was funded, after a call for applications for research, by a grant from the Health Services Research Committee at the SLaM NHS trust. The second larger study (Connolly & Taylor, 2008) was then funded after application to the trustees of the charitable fund of the SLaM NHS trust. Publication and dissemination of the results of these earlier studies through conference presentations resulted in an approach with funding for this national study from the Equality and Human Rights Commission (previously the Commission for Racial Equality).

2.2 Method

2.2.1 Study Design and Setting

The study was a cross-sectional survey of antipsychotic prescribing in black and white inpatients prescribed one or more regular antipsychotics on the day of the data collection. It was conducted at eight mental health trusts across the UK.

2.2.2 SUBJECTS

Inclusion criteria:

- All adult inpatients (aged 18 and over) on acute general psychiatry wards, including psychiatric intensive care units.
- Prescribed one or more regular antipsychotics on the day of the data collection (or had received a when required/ PRN dose in the last 24 hours).

Exclusion criteria:

- All suitable patients within each trust were included over a three-month period: none were excluded except for reasons above.

Recording of ethnicity is mandatory for all inpatients (Department of Health, 2007) and patients were classed as white (white British, white Irish, white other), black (black British, black African, black Caribbean, black other), mixed (white and black Caribbean, white and black African, white and Asian, mixed other), Asian (Asian British, Asian Indian, Asian Pakistani, Asian other) or Chinese/other ethnic group according to their medical notes (as categorised by the Office for National Statistics (Office for National Statistics, 2001)). As discussed in Chapter 1, classification of ethnicity aims to include the variability and complexity of people but research requires categorisation. The ethnic groups used by the Office for National Statistics contain diverse collections of people. Collapsing of ethnic categories loses heterogeneity and can ultimately affect results.

This study differed from the previous ones in that data were collected on all ethnicities not only black or white patients (Connolly et al., 2007; Connolly & Taylor, 2008). Analysis of the data in this chapter is for black and white patients only – the two largest ethnic groups in the population sample.

2.2.3 DATA COLLECTION

Ten mental health trusts were approached to take part in this survey of antipsychotic prescribing and ethnicity. These trusts were chosen because they served populations known to have the largest proportions of BME patients in the UK. Data from the 'Count me in Census' by the Care Quality Commission (Care Quality Commission, 2009) (see Chapter 1 for discussion of this document) were used to determine which UK mental health trusts had the most ethnically diverse patient population (see Appendix 13). Multiple efforts were made to contact and encourage these trusts to contribute to the data collection. Trusts were initially invited to take part by written contact with their chief pharmacist. Those who did not reply were contacted once again by letter and then by telephone. Finally if there was still no reply the funding agency supporting the research (Equality and Human Rights Commission) was contacted so that they could follow up non-responding trusts through their regular meetings with NHS trust Chief Executives. Contact with each trust highlighted the benefits of engaging in the study which included:

- Analysis of data on antipsychotic prescribing and ethnicity for their trust.
- Comparison of their results with other English mental health trusts.
- A financial contribution towards the cost of data collection.
- Assistance and support with engaging in multicentre audit.
- Suggestions on how to improve equality of prescribing practice.

The funding from the Equality and Human Rights Commission was used to provide financial assistance to the NHS trusts taking part to cover costs of data collection.

2.2.4 OUTCOMES

Prescribing outcomes have been well studied in psychiatry. Quality standards have been set nationally in the UK by the Prescribing Observatory for Mental Health and are audited regularly (Paton et al., 2008). There here have been many studies of antipsychotic prescribing and ethnicity completed worldwide (see Chapter 1). The quality standards from POMH-UK and other studies of ethnicity and antipsychotics were used as outcome measures.

The main outcomes of the study were:

- Dose - expressed as a percentage of the BNF licensed maximum dose (British Medical Association and Royal Pharmaceutical Society of Great Britain, 2008).
- High dose - being prescribed antipsychotic medication above maximum BNF doses i.e. at more than 100% of the BNF maximum dose (British Medical Association and Royal Pharmaceutical Society of Great Britain, 2008).
- Polypharmacy prescribed - more than one antipsychotic prescribed regularly or when required.
- Polypharmacy administered - more than one antipsychotic prescribed and administered in the last 24 hours.
- Type of antipsychotic - categories of FGA and SGA from the BNF (British Medical Association and Royal Pharmaceutical Society of Great Britain, 2008).
- Cost - 28 days of medication (Monthly Index of Medical Specialities, December 2008).

2.2.5 INSTRUMENTS AND PERSONNEL

Data were collected by pharmacists or doctors working within each NHS trust during normal working hours, as part of routine clinical care. Each data collector was visited in person and trained by the researcher on how and where to collect the data from and an

explanation of data collection definitions provided. This information was also provided in written form (Appendices 10, 11 and 12) and telephone contact support for the data collectors was also offered.

Potential confounders were predetermined from previous research (see Appendix 2), previous studies I have conducted and published in peer-reviewed journals and expert opinion (medical and pharmacist colleagues experienced in ethnicity research methodology and statistics) as described above and are listed in Table 4. The confounders were defined for the data collectors as in Appendix 10. They were determined by reference to casenotes, prescription charts and to standard reference texts for dose, type and cost (British Medical Association and Royal Pharmaceutical Society of Great Britain, 2008; Monthly Index of Medical Specialities, December 2008).

TABLE 4 POTENTIAL CONFOUNDERS

Type of data	**Confounder**
Demographic	Age, gender, education, employment status, forensic history (previous conviction or currently charged with an offence), language spoken, smoking status, ethnicity of patient's consultant.
Clinical	Current legal detention status, current substance misuse, diagnosis, duration of illness, length of current admission, number of previous admissions, history of or current non-compliance, weight.
Medication-specific	Previous antipsychotic treatments, previous treatment with current antipsychotic medication, anticholinergic prescribed regularly, length of current antipsychotic treatment, route of administration.
Outcome-based	Dose, high dose, polypharmacy prescribed, polypharmacy administered, type of antipsychotic, cost of antipsychotic.

2.2.6 SAMPLE SIZE

A 'power' calculation was performed before starting the study to avoid a false negative type II statistical error (Jones et al., 2003). A sample size of 788 was calculated to be required to have an 80% chance of detecting a 5% (55% vs. 50%) absolute difference for the main outcome (percentage maximum dose) between black and white patients (assuming a standard deviation of 25). Estimates of dose and standard deviation were taken from previous studies on ethnicity and prescribing (Connolly et al., 2007; Connolly & Taylor, 2008).

2.2.7 Statistical Analysis

The aim was to compare the six outcomes between the two groups (black and white patients) and to adjust the resulting comparisons for the effect of confounding variables. Although the trust caring for the patient was not included as a confounder in this data analysis it was used in later analyses to compare how prescribing practice varied by centre (see Chapter 3). Data collection forms were quality assured for accuracy and completeness before entry onto a database and then the database was again checked against paper records after all the data had been entered.

Baseline demographic and clinical characteristics were analysed by ethnicity. A linear regression model was then used to investigate whether there was a difference between black and white patients for the continuous outcomes of dose and cost of treatment. Confounding variables to be included in the model were selected using a stepwise forward selection procedure with a selection criterion of 10% and removal criterion of 20%. Where the relationship between continuous potential confounding variables and the outcomes could not be assumed to be linear (a requirement for regression modelling (Field, 2013)) and transforming variables did not induce a linear relationship, restricted cubic splines were applied. The fit of each model and the influence of observations were examined. This modelling produced an adjusted effect size (i.e. median percentage difference for dose and median cost difference) for ethnicity for the outcomes of dose and cost. A similar approach was used for the binary outcomes of high dose, polypharmacy prescribed, polypharmacy administered and prescribing of FGA drugs, but using logistic regression modelling. This modelling allowed the calculation of adjusted odds ratios. Identification of confounding variables was as described above. The fit of each model was examined using residual analysis.

Initially a complete case analysis was performed for each of the regression models i.e. where only patients with complete covariate data were included in the model. Excluding patients without full information may result in biased estimates. Consequently values were imputed for patients with missing covariate data using a multiple imputation method. For each variable an appropriate regression model was specified. Five datasets containing imputed values were created then each data set was analysed and the relevant parameters were averaged across the data to give a single estimate. The analysis was performed using the function ICE in Stata version 10. The adjusted results reported are for the imputed data sets.

2.2.8 Ethical Committee Approval

Individual trust approvals were sought and obtained for the study through local clinical audit channels. All data were anonymised at source and participants were not identifiable.

2.2.9 Hypothesis

The null hypothesis was black patients are prescribed the same total dose of antipsychotics as white.

2.2.10 Aim

The purpose of the study was to discover if black patients receive different doses (total dose, high dose) or treatment (type, number, cost) of antipsychotics compared with white patients.

2.2.11 Objectives

- To complete a study of antipsychotic prescribing and ethnicity
- To collect multiple potentially confounding factors that may be affecting the outcomes
- To analyse the black and white ethnicity data statistically to determine if ethnicity influences any of the study's outcomes

2.3 Results

2.3.1 Primary Outcome-complete Case Analysis

Nine trusts agreed to take part and eight (Barnet, Enfield and Haringey, Camden and Islington, Central and North West London, East London and City, Manchester Mental Health and Social Care Trust, North East London, Nottinghamshire Healthcare, South London and Maudsley) completed the data collection. Data relating to 938 patients across eight centres was collected of which 541 (57.7%) were white and 397 (42.3%) black. The demographic data, including clinical information, and numbers recruited from each centre are displayed in Tables 5 and 6. The largest number of patients came from SLaM, most were male, middle-aged, unemployed, had completed their secondary education, spoke English as a first language and smoked cigarettes. Clinically a greater number had schizophrenia, weighed more than 77kg, were compulsorily detained in hospital, did not have a forensic history, had had two or more hospital admissions, a duration of illness of at least 8 years, a length of admission of more than 8 weeks, a history of non-compliance with medication and were not misusing substances. Most had a consultant of white ethnicity and a third of senior doctors were from a minority ethnic group. For the medication-specific confounders most patients had taken their current antipsychotic before and two or more antipsychotics previously, were taking treatment

orally, had been on their current treatment for 40 days or more and were not taking an anticholinergic medicine.

Not all confounder data were available for all subjects at the time of the survey. Total missing data proportions by centre are listed in Table 7. The proportion of primary outcome-complete confounder data were 94.6% (18627 complete data points) and main outcome data (percentage maximum dose) 100%; missing data were imputed as described earlier.

TABLE 5 DEMOGRAPHIC AND CLINICAL CATEGORIES BY ETHNICITY

Variable (n = complete)	**White n=541(%)**	**Black n=397 (%)**
Centre (938)		
SLaM	88 (44.2)	111 (55.8)
CNWL	91 (61.5)	57 (38.5)
ELC	45 (37.2)	76 (62.8)
BEH	51 (46.8)	58 (53.2)
C&I	59 (60.2)	39 (39.8)
NEL	68 (72.3)	26 (27.7)
Manchester	73 (82)	16 (18)
Nottingham	66 (82.5)	14 (17.5)
Gender (938)		
Male	323 (59.7)	267 (67.3)
Female	218 (40.3)	130 (32.7)
Employment (921)		
Unemployed	475 (90.5)	360 (90.9)
Employed	22 (4.2)	18 (4.5)
Student	5 (0.9)	16 (4)
Retired	23 (4.4)	2 (0.5)
Education (858)		
Primary	67 (13.9)	48 (12.7)
Secondary	276 (57.3)	205 (54.1)
6th form/to 18 years	95 (19.7)	91 (24)
University	44 (9.1)	35 (9.2)
Language (916)		
Not English	41 (7.9)	48 (12.2)
English	481 (92.1)	346 (87.8)
Smoking status (896)		
Smoker	389 (76.9)	265 (67.9)
Non-smoker	117 (23.1)	125 (32.1)
Diagnosis (875)		
Schizophrenia	314 (64.3)	306 (79.1)
Other	174 (35.7)	81 (20.9)
Ethnicity of Consultant (912)		
White	358 (67.5)	254 (66.5)
Mixed	6 (1.1)	4 (1)
Asian	75 (14.2)	45 (11.8)
Black	60 (11.3)	56 (14.7)
Chinese/other	31 (5.8)	23 (6)
Previous treatment with current antipsychotic (841)		
Yes	292 (62.4)	248 (66.5)

Variable (n=complete)	White n=541(%)	Black n=397 (%)
Legal Status (934)		
Informal	199 (37.1)	92 (23.2)
Sectioned (compulsorily detained in hospital)	338 (62.9)	305 (76.8)
Forensic History (863)		
Yes	179 (37.1)	191 (50.1)
Previous antipsychotics (812)		
None	92 (20.5)	86 (23.6)
1	116 (25.9)	71 (19.5)
2 to 5	203 (45.3)	181 (49.7)
≥ 6	37 (8.3)	26 (7.1)
Previous admissions (871)		
None	46 (9.5)	48 (12.4)
1	48 (9.9)	44 (11.3)
2 to 5	172 (35.6)	151 (38.9)
≥ 6	217 (44.9)	145 (37.4)
Non-compliance history (874)		
Yes	373 (76.1)	322 (83.9)
Route (938)		
Oral	432 (79.9)	280 (70.5)
Intramuscular	109 (20.1)	117 (29.5)
Regular anticholinergic use (918)		
Yes	86 (16.3)	65 (16.6)
Substance misuse (892)		
Yes	216 (43)	188 (48.2)

TABLE 6 CONTINUOUS DEMOGRAPHIC AND CLINICAL CATEGORIES BY ETHNICITY

Variable (n=complete)	White (n=541)	Black (n=397)
Median **age** in years (95% confidence interval (CI)), n=938	42 (40, 43)	35 (33, 37)
Median **duration of illness** in days (95% CI), n=840	3950 (3387, 4380)	2920 (2190, 3285)
Median **weight** in kilograms (95% CI), n=833	77 (75, 79)	80 (78, 83)
Median **length of admission** in days (95% CI), n=926	57 (49, 62)	58 (50, 67)
Median **length of treatment with current antipsychotic** in days (95% CI), n=831	40 (31, 46)	40 (35, 51)

TABLE 7 TOTAL MISSING DATA BY CENTRE

Centre	**Complete data cases (%)**	**Cases with at least one variable missing (%)**	**Total cases (%)**
SLaM	190 (95.5)	9 (4.5)	199 (21.2)
CNWL	94 (63.5)	54 (36.5)	148 (15.8)
ELC	107 (88.4)	14 (11.6)	121 (12.9)
BEH	100 (91.7)	9 (8.3)	109 (11.6)
C&I	91 (92.9)	7 (7.1)	98 (10.4)
NEL	29 (30.8)	65 (69.2)	94 (10)
Manchester	11 (12.4)	78 (87.6)	89 (9.5)
Nottingham	78 (97.5)	2 (2.5)	80 (8.5)
Total	**700 (74.6)**	**238 (25.3)**	**938 (100)**

Outcomes (with histograms where appropriate) are described in Figures 3 through to 12. Both percentage maximum dose and cost outcomes were skewed so median values were used in preference to mean for accuracy. There significant differences were not found in any outcome by ethnicity.

FIGURE 3 TOTAL PERCENTAGE MAXIMUM DOSE WHITE ETHNICITY

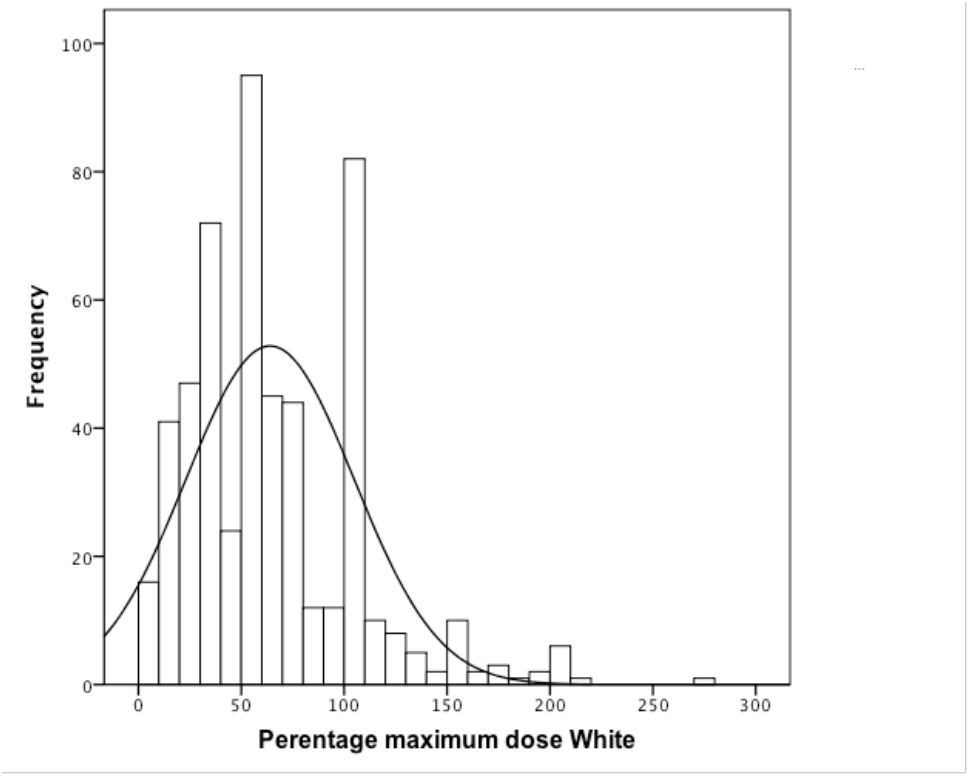


FIGURE 4 TOTAL PERCENTAGE MAXIMUM DOSE BLACK ETHNICITY

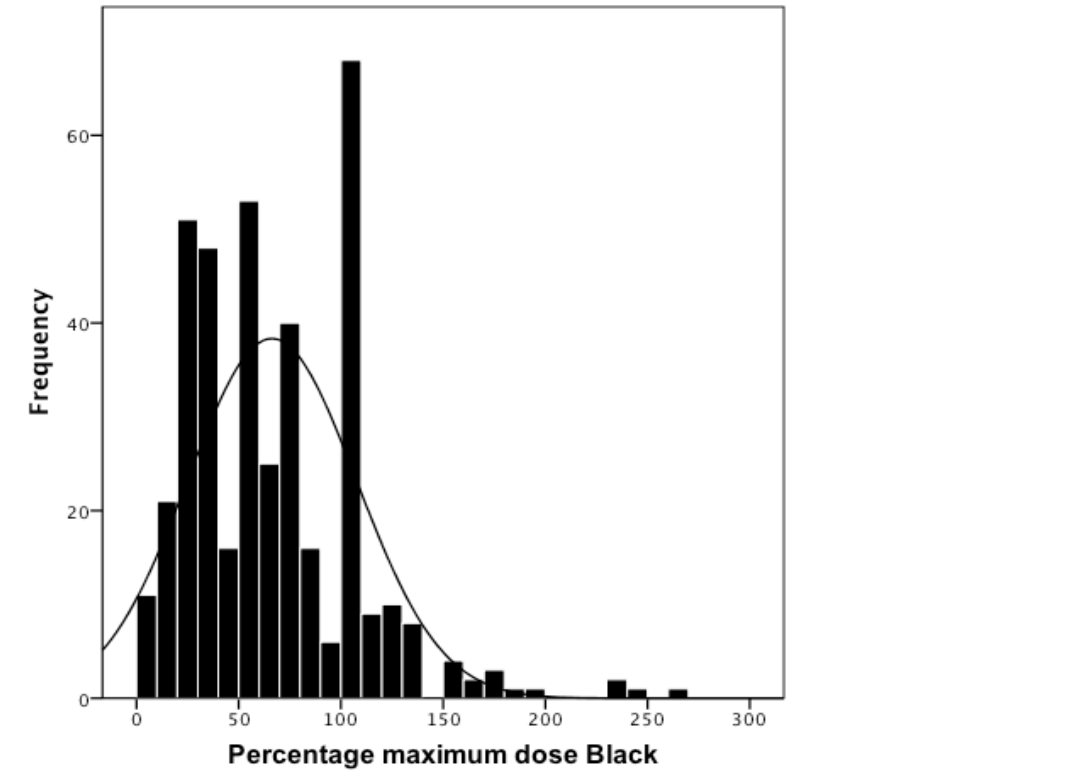
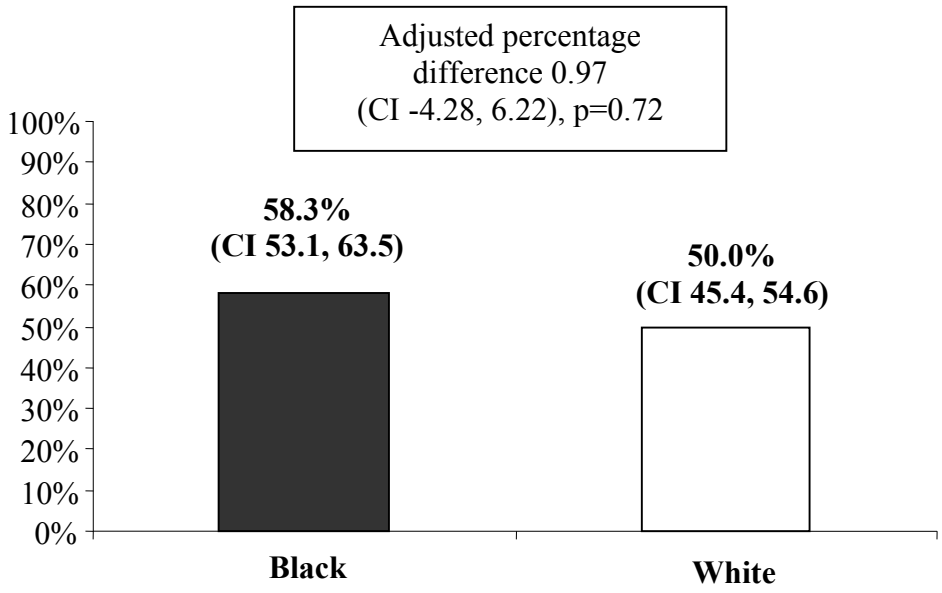
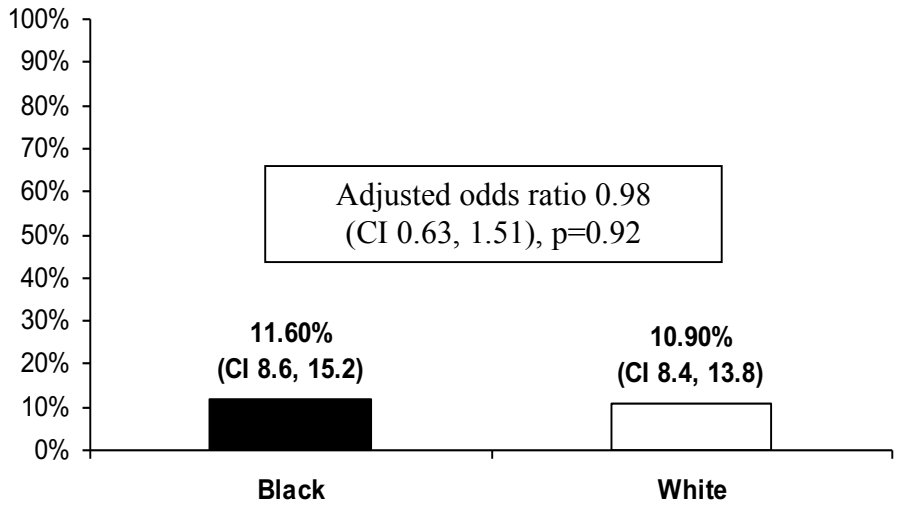


FIGURE 5 MEDIAN PERCENTAGE MAXIMUM DOSE



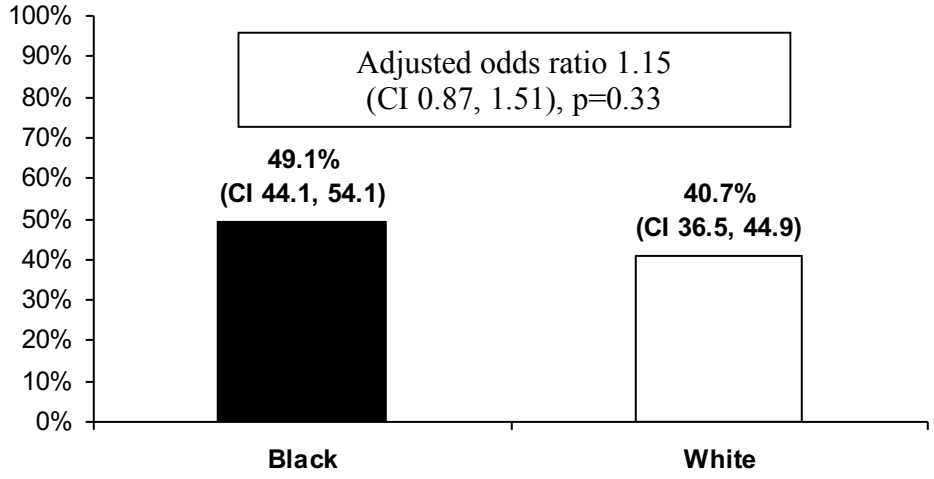
Unadjusted percentage difference 2.28 (CI -3.04, 7.61), p=0.4

FIGURE 6 PROPORTION RECEIVING HIGH DOSE (>100% MAXIMUM DOSE)



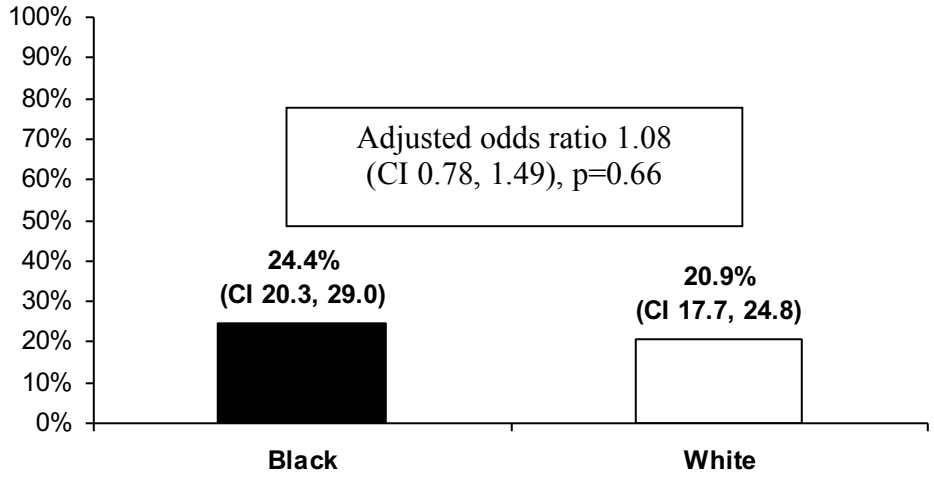
Unadjusted odds ratio 1.07 (CI 0.71, 1.61), p=0.74

FIGURE 7 PROPORTION PRESCRIBED POLYPHARMACY



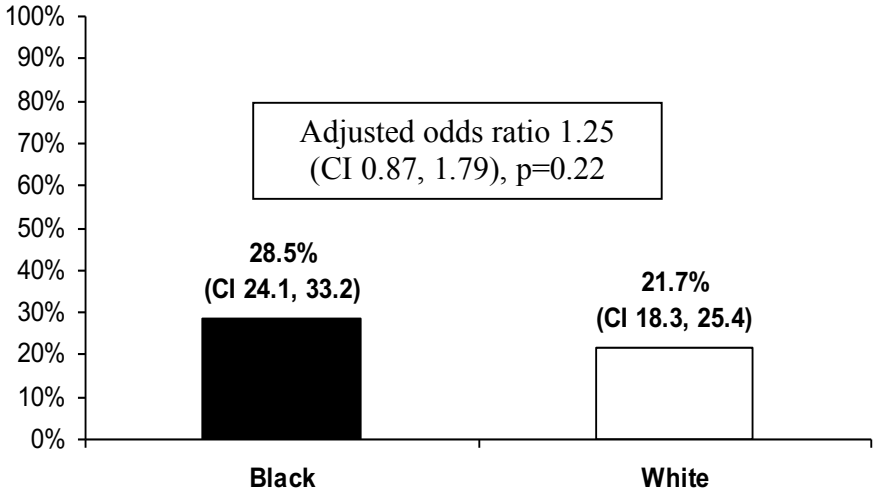
Unadjusted odds ratio 1.41 (CI 1.08, 1.83), p=0.01

FIGURE 8 PROPORTION ADMINISTERED POLYPHARMACY



Unadjusted odds ratio 1.22 (CI 0.9, 1.67), p=0.2

FIGURE 9 PROPORTION PRESCRIBED A FIRST GENERATION ANTIPSYCHOTIC



Unadjusted odds ratio 1.44 (CI 1.06, 1.94), p=0.02

FIGURE 10 COST (£) OF 28 DAYS ANTIPSYCHOTIC TREATMENT FOR WHITE ETHNICITY

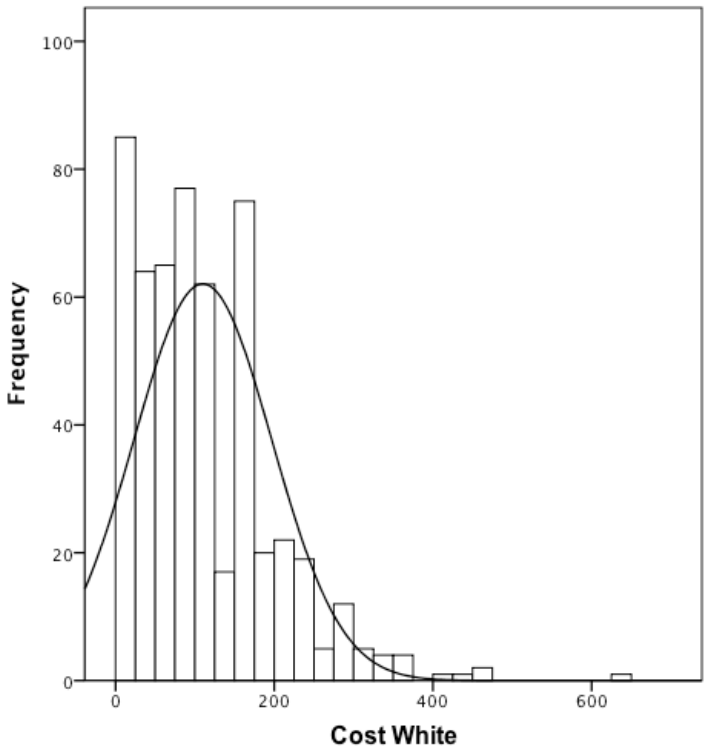


FIGURE 11 COST (£) OF 28 DAYS ANTIPSYCHOTIC TREATMENT FOR BLACK ETHNICITY

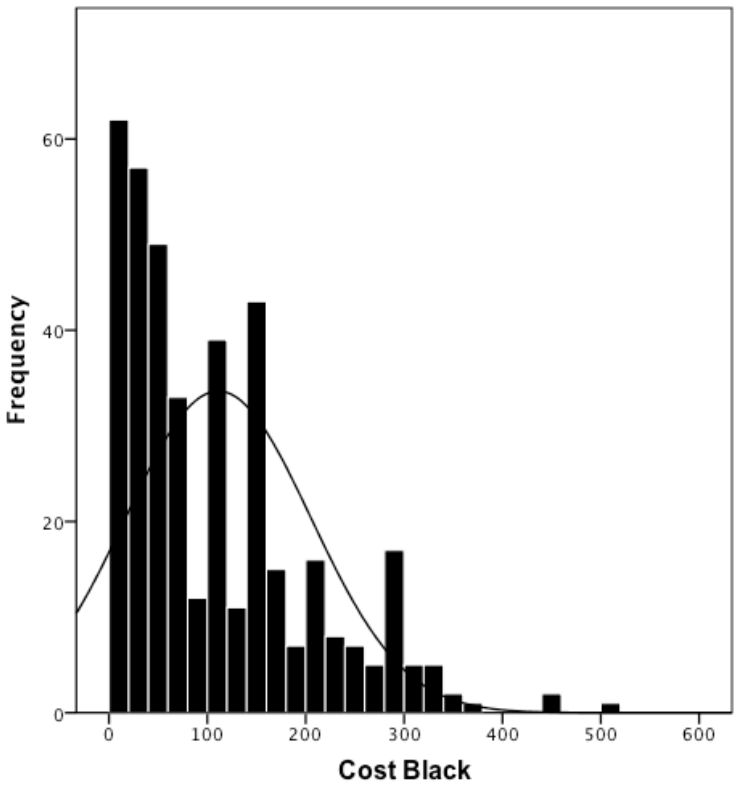
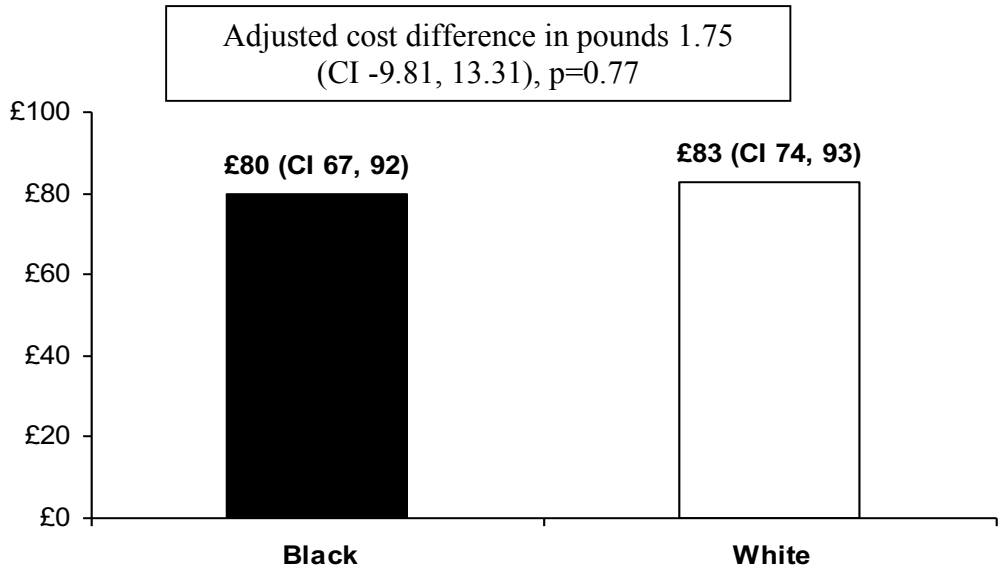


FIGURE 12 MEDIAN COST (£) OF 28 DAYS ANTIPSYCHOTIC TREATMENT



Unadjusted cost difference in pounds 1.08 (CI -10.6, 12.8), p=0.86

Key for Figures: * calculated as percentage maximum dose; CI = 95% confidence interval; ratios expressed as black compared with white (reference category).

Each outcome model was adjusted for multiple confounders. The final models are displayed in Tables 8 through to 13.

The unadjusted values quoted on the graphs for dose (Figure 5) and cost (Figure 12) represent the regression coefficients from the fitted linear regression models. These are median values. The differences between adjusted and unadjusted values are because of the outcome data being skewed. The residuals of the regression model were deemed to be normally distributed.

TABLE 8 LINEAR REGRESSION MODEL FOR MEDIAN TOTAL PERCENTAGE MAXIMUM DOSE (PRIMARY OUTCOME-COMPLETE, N=938)

Variable	**Coefficient**	**Standard Error**	**p value**	**95% CI**
Ethnicity: black	0.97	2.67	0.72	-4.28, 6.22
Previous treatment with current antipsychotic: yes	12.80	3.00	<0.001	6.90, 18.70
Legal status: sectioned	5.04	2.85	0.08	-0.56,10.64
Previous admissions: more than 5	3.37	1.51	0.03	0.40, 6.34
Gender: female	-7.80	2.77	0.005	-13.24, -2.37
Length of admission (log)	4.84	0.97	<0.001	2.93, 6.74
Route: intramuscular	-2.78	3.10	0.37	-8.86, 3.31
Weight 1	0.16	0.34	0.63	-0.51, 0.84
Weight 2	1.17	1.11	0.30	-1.05, 3.40
Weight 3	-5.85	3.78	0.13	-13.37, 1.67
Ethnicity of consultant: black	10.20	20.52	0.62	-30.69, 51.10

Some variables violated an assumption of linear regression that there must be a linear relationship between outcome and confounder. These were transformed and included in the model using the log scale for the length of admission in days and restricted cubic splines (a third order polynomial equation) using four knots (where polynomial sections join) equally spaced for the weight variable.

Variables with significant influence on dose were: patients who had previously received treatment with their current antipsychotic had a 12.80% higher dose; those who had more than five previous hospital admissions had a 3.37% higher dose; females had a 7.8% lower dose and those with a longer length of hospital stay had a 1.58% (i.e. log 4.84) higher dose.

TABLE 9 LOGISTIC REGRESSION MODEL FOR HIGH DOSE (PRIMARY OUTCOME-COMPLETE, N=938)

Variable	**Odds Ratio (OR)**	**Standard Error**	**p value**	**95% CI**
Ethnicity: black	0.98	0.22	0.92	0.63, 1.51
Weight (kg)*	1.01	0.01	0.06	1.00, 1.02
Education: A level/up to age 18	0.54	0.17	0.06	0.29, 1.01
Diagnosis: not schizophrenia	0.55	0.19	0.09	0.28, 1.10
Ethnicity of consultant: black	2.29	0.56	0.001	1.42, 3.69
Legal status: sectioned	1.08	0.26	0.77	0.66, 1.74
Previous treatment with current antipsychotic: yes	2.70	0.80	0.001	1.50, 4.86

*OR for 1kg weight change

For prescribing of high dose, patients whose consultant's ethnicity was black had more than twice the odds of receiving a high dose compared with white consultants. In addition those previously treated with their current antipsychotic also had more than twice the odds of receiving a high dose compared with those who had not had their current treatment before.

TABLE 10 LOGISTIC REGRESSION MODEL FOR POLYPHARMACY PRESCRIBED (PRIMARY OUTCOME-COMPLETE CASES, N=938)

Variable	**Odds Ratio (OR)**	**Standard Error**	**p value**	**95% CI**
Ethnicity: black	1.15	0.16	0.33	0.87, 1.51
Age (years)*	0.98	0.01	0.002	0.97, 0.99
Legal status: sectioned	1.61	0.24	0.001	1.20, 2.16
Route: intramuscular	1.42	0.22	0.02	1.05, 1.94
Previous treatment with current antipsychotic: yes	1.84	0.27	<0.001	1.39, 2.46
Ethnicity of consultant: black	1.03	0.21	0.87	0.69, 1.55
Employment: student	0.47	0.22	0.11	0.19, 1.18

*OR for change per increase in years

Each year increase in age reduced the odds of being prescribed polypharmacy by 2%. Being detained under the Mental Health Act, receiving an intramuscular antipsychotic and having previously been treated with their current antipsychotic increased the odds of prescribed polypharmacy.

TABLE 11 LOGISTIC REGRESSION MODEL FOR POLYPHARMACY ADMINISTERED (PRIMARY OUTCOME-COMPLETE CASES, N=938)

Variable	**Odds Ratio (OR)**	**Standard Error**	**p value**	**95% CI**
Ethnicity: black	1.08	0.18	0.66	0.78, 1.49
Age (years)*	0.98	0.007	0.001	0.96, 0.99
Education: secondary	1.70	0.29	0.002	1.22, 2.38
Legal status: sectioned	1.18	0.22	0.38	0.82, 1.69
Previous admissions: more than 5	1.25	0.13	0.04	1.02, 1.55
Route: intramuscular	1.82	0.32	0.001	1.28, 2.57
Previous treatment with current antipsychotic: yes	2.02	0.46	0.004	1.28, 3.20

*OR for change per increase in years

Each year increase in age reduced the odds of being administered polypharmacy by 2%. Being educated to secondary level (compared with primary), a higher number of previous admissions, receiving an intramuscular antipsychotic and having previously been treated with their current antipsychotic all increased the odds of administered polypharmacy.

TABLE 12 LOGISTIC REGRESSION MODEL FOR FIRST GENERATION TYPE OF ANTIPSYCHOTIC (PRIMARY OUTCOME-COMPLETE CASES, N=938)

Variable	**Odds Ratio (OR)**	**Standard Error**	**p value**	**95% CI**
Ethnicity: black	1.25	0.23	0.22	0.87, 1.79
Route: intramuscular	10.75	2.01	0.001	7.45, 15.51
Anticholinergic use: no	0.24	0.05	0.001	0.16, 0.37
Previous treatment with current antipsychotic: yes	1.33	0.27	0.16	0.89, 1.96
Ethnicity of consultant: black	0.52	0.16	0.03	0.28, 0.95

Receiving an intramuscular antipsychotic was associated with a ten-fold increase in odds of taking a FGA. Not taking an anticholinergic and having a consultant of black ethnicity reduced the odds of taking a FGA.

TABLE 13 LINEAR REGRESSION MODEL FOR MEDIAN COST (PRIMARY OUTCOME-COMPLETE CASES, N=938)

Variable	**Coefficient**	**Standard Error**	**p value**	**95% CI**
Ethnicity: black	1.75	5.89	0.77	-9.81, 13.31
Weight 1	0.04	0.71	0.96	-1.38, 1.45
Weight 2	2.92	2.30	0.21	-1.61, 7.44
Weight 3	-13.92	7.85	0.08	-29.35, 1.50
Previous admissions: more than 5	6.64	3.33	0.05	-0.10, 13.19
Anticholinergic use: no	25.93	7.86	0.001	10.51, 41.35
Previous treatment with current antipsychotic: yes	17.16	6.69	0.01	3.98, 30.34
Length of admission (log)	9.36	2.16	0.001	5.12, 13.60
Ethnicity of consultant: black	6.62	44.44	0.88	-81.41, 94.66

As with the dose outcome, some variables violated an assumption of linear regression that there must be a linear relationship between outcome and confounder. These were transformed and included in the model using the log scale for the length of admission in days and restricted cubic splines (a third order polynomial equation) using four knots (where polynomial sections join) equally spaced for the weight variable. Variables with

significant influence on cost were those patients who were not taking an anticholinergic who had a 25.93% higher cost; those who had previously received treatment with their current antipsychotic had a 17.16% higher dose; those with a longer length of admission had a 2.24% (i.e. log 9.36) higher cost.

2.3.2 COMPLETE CASE ANALYSIS

TABLE 14 LINEAR REGRESSION MODEL FOR MEDIAN TOTAL PERCENTAGE MAXIMUM DOSE (COMPLETE CASES N=790)

Variable	**Coefficient**	**Standard Error**	**p value**	**95% CI**
Ethnicity: black	0.16	2.85	0.96	-5.43, 5.75
Previous treatment with current antipsychotic: yes	15.09	3.06	<0.001	9.07, 21.10
Legal status: sectioned	6.84	3.11	0.03	0.73, 12.96
Previous admissions: more than 5	3.78	1.59	0.02	0.67, 6.89
Gender: female	-6.60	3.01	0.03	-12.51, -0.70
Length of admission (log)	5.20	1.05	<0.001	3.14, 7.25
Route: intramuscular	-5.12	3.34	0.13	-11.68, 1.45
Weight 1	0.27	0.33	0.41	-0.37, 0.91
Weight 2	1.18	1.13	0.30	-1.05, 3.40
Weight 3	-6.04	3.77	0.11	-13.45, 1.36
Ethnicity of consultant: black	-2.32	20.94	0.91	-43.44, 38.79

Variables with significant influence on dose were those patients who had previously received treatment with their current antipsychotic had a 15.09% higher dose; were detained under the Mental Health Act had a 6.84% higher dose; who had more than five previous hospital admissions had a 3.78% higher dose; who were female had a 6.6% lower dose; with a longer length of admission had a 1.65% (i.e. log 5.2) higher dose.

TABLE 15 LOGISTIC REGRESSION MODEL FOR HIGH DOSE (COMPLETE CASES, N=762)

Variable	**Odds Ratio (OR)**	**Standard Error**	**p value**	**95% CI**
Ethnicity: black	0.89	0.21	0.62	0.55, 1.42
Weight (kg)*	1.02	0.01	0.01	1.01, 1.03
Education: A level/up to age 18	0.57	0.19	0.09	0.30, 1.08
Diagnosis: not schizophrenia	0.51	0.17	0.04	0.27, 0.97
Ethnicity of consultant: Chinese/other	2.40	0.66	0.002	1.40, 4.11
Legal status: sectioned	1.62	0.47	0.10	0.92, 2.85
Previous treatment with current antipsychotic: yes	2.99	0.91	<0.001	1.64, 5.45

*OR for 1kg weight change

For the prescribing of high dose, each 1 kg increase in weight was associated with a 2% increase in the odds of receiving a high dose. Patients without schizophrenia have approximately half the odds of receiving a high dose and those whose medical consultants ethnicity is Chinese/other have twice the odds of being prescribed a high dose compared with those patients with a white consultant. Patients who have previously been treated with their current antipsychotic have approximately three-times the odds of receiving a high dose.

TABLE 16 LOGISTIC REGRESSION MODEL FOR POLYPHARMACY PRESCRIBED (COMPLETE CASES, N=813)

Variable	**Odds Ratio (OR)**	**Standard Error**	**p value**	**95% CI**
Ethnicity: black	1.06	0.16	0.70	0.79, 1.43
Age (years)*	0.98	0.006	0.001	0.97, 0.99
Legal status: sectioned	1.54	0.25	0.008	1.12, 2.13
Route: intramuscular	1.31	0.22	0.12	0.94, 1.83
Previous treatment with current antipsychotic: yes	1.94	0.30	0.001	1.43, 2.63
Ethnicity of consultant: black	1.32	0.30	0.22	0.85, 2.06
Employment: student	0.41	0.21	0.08	0.15, 1.13

*OR for change per increase in years

For this outcome, each year increase in age reduced the odds of being prescribed polypharmacy by 2%. Being detained under the Mental Health Act and having previously been treated with their current antipsychotic increased the odds of prescribed polypharmacy.

TABLE 17 LOGISTIC REGRESSION MODEL FOR POLYPHARMACY ADMINISTERED (COMPLETE CASES, N=803)

Variable	**Odds Ratio (OR)**	**Standard Error**	**p value**	**95% CI**
Ethnicity: black	1.08	0.18	0.66	0.78, 1.49
Age (years)*	0.98	0.007	0.001	0.96, 0.99
Education: secondary	1.70	0.29	0.002	1.22, 2.38
Legal status: sectioned	1.18	0.22	0.38	0.82, 1.69
Previous admissions: more than 5	1.25	0.13	0.04	1.02, 1.55
Route: intramuscular	1.82	0.32	0.001	1.28, 2.57
Previous treatment with current antipsychotic: yes	2.02	0.46	0.004	1.28, 3.20

*OR for change per increase in years

Each year increase in age reduced the odds of being administered polypharmacy by 2%. Being educated to secondary level (compared with primary), a higher number of previous admissions, receiving an intramuscular antipsychotic and having previously been treated with their current antipsychotic all increased the odds of administered polypharmacy.

TABLE 18 LOGISTIC REGRESSION MODEL FOR FIRST GENERATION TYPE OF ANTIPSYCHOTIC (COMPLETE CASES, N=794)

Variable	**Odds Ratio (OR)**	**Standard Error**	**p value**	**95% CI**
Ethnicity: black	1.10	0.22	0.63	0.74, 1.63
Route: intramuscular	12.16	2.52	0.001	8.11, 18.25
Anticholinergic use: no	0.21	0.05	0.001	0.13, 0.34
Previous treatment with current antipsychotic: yes	1.44	0.31	0.09	0.95, 2.20
Ethnicity of consultant: black	0.47	0.16	0.03	0.24, 0.93

Receiving an intramuscular antipsychotic was associated with a twelvefold increase in odds of taking a FGA. Not taking an anticholinergic and having a consultant of black ethnicity reduced the odds of taking a FGA.

TABLE 19 LINEAR REGRESSION MODEL FOR MEDIAN COST (COMPLETE CASES, N=790)

Variable	**Coefficient**	**Standard Error**	**p value**	**95% CI**
Ethnicity: black	2.03	6.26	0.75	-10.25, 14.31
Weight 1	0.22	0.71	0.76	-1.18, 1.63
Weight 2	2.85	2.53	0.26	-2.12, 7.81
Weight 3	-13.92	8.41	0.10	-30.43, 2.59
Previous admissions: more than 5	6.68	3.49	0.06	-0.17, 13.52
Anticholinergic use: no	28.20	8.55	0.001	11.41, 44.99
Previous treatment with current antipsychotic: yes	20.77	6.84	0.002	7.35, 34.20
Length of admission (log)*	10.17	2.30	0.001	5.65, 14.68
Ethnicity of consultant: black	-15.70	45.90	0.73	-105.80, 74.39

*OR for change in 100 days

Variables with significant influence on cost were those patients who were not taking an anticholinergic who had a 28.20% higher cost; those who had previously received treatment with their current antipsychotic had a 20.77% higher cost; those with a longer length of admission had a 2.32% (i.e. log 10.17) higher cost.

2.3.3 ROUTE OF ADMINISTRATION

Injectable preparations accounted for approximately a quarter of those prescribed. black patients were more likely than white to receive an intramuscular antipsychotic (chi-squared test, p=0.001). Route of administration by ethnicity was analysed using logistic regression in Chapter 4.

2.3.4 INDIVIDUAL ANTIPSYCHOTICS

Risperidone (oral plus intramuscular) and olanzapine were prescribed most frequently and zotepine the least (see Table 20). Clozapine use accounted for 10% of the frequency of prescribing of antipsychotics and did not differ by ethnicity for black and white patients (chi-squared test, p= 0.287) (see Chapter 4 also).

TABLE 20 FREQUENCY OF ANTIPSYCHOTICS PRESCRIBED

Antipsychotic	**Ethnicity**		**Frequency (%)**	
	White	**Black**		
Risperidone oral	78	77	155 (15.9)	Total 243 (25)
Risperidone long-acting injection	43	45	88 (9.1)	
Olanzapine oral	154	83	237 (24.4)	
Clozapine	61	36	97 (10)	
Quetiapine	60	25	85 (8.7)	
Haloperidol oral	23	24	47 (4.8)	Total 71 (7.3)
Haloperidol decanoate injection	8	15	23 (2.4)	
Haloperidol aqueous injection	0	1	1 (0.1)	
Zuclopentixol decanoate injection	30	26	56 (5.9)	Total 59 (6.2)
Zuclopentixol oral	2	1	3 (0.3)	
Aripiprazole	26	18	44 (4.5)	
Pipotiazine palmitate injection	16	19	35 (3.6)	
Amisulpride	19	8	27 (2.8)	
Flupentixol decanoate injection	13	12	25 (2.6)	
Flupentixol oral	2	0	2 (0.2)	
Chlorpromazine	8	7	15 (1.5)	
Trifluoperazine	6	5	11 (1.1)	
Fluphenazine decanoate injection	5	4	9 (0.9)	
Sulpiride	5	4	9 (0.9)	
Zotepine	3	0	3 (0.3)	
Total	**562**	**410**	**972**	

2.4 DISCUSSION

2.4.1 MAIN FINDINGS

In this multicentre study of antipsychotic prescribing practice in black and white patients, involving a large cohort drawn from across the UK, significant differences were not found between the two groups for dose, high dose, polypharmacy, type, route and cost of treatment, after adjustment for multiple confounding factors. The numerous

associations found between potential confounders and outcomes confirms the importance of adjustment for these factors. Nonetheless significant limitations may have affected these results.

2.4.2 Population

Our population were inpatients in acute psychiatric care in mental health trusts with high proportions of black and minority ethnic groups in England. Thus results could be applied to the larger population of UK inpatients. Community patients were not included which may have affected the results. Patients not in hospital are usually less acutely unwell and so are likely to be on stable doses of medication for longer periods. If community patients had been included in the study they may have provided more accurate data on dose, high dose and the true extent of polypharmacy because PRN prescribing for rapid tranquillisation would have been eliminated. Indeed a recent study of antipsychotic use by ethnicity in a large community sample (Das-Munshi et al., 2018) found that black patients, compared with white, were more likely to be prescribed depot antipsychotics and were less likely to be prescribed clozapine. Mixed patients were more likely than white to receive high dose antipsychotic treatment.

2.4.3 Variables associated with each outcome

The two different data sets analysed (primary outcome-complete and complete cases) produced broadly similar results. Each outcome was adjusted for different variables. These are discussed in detail below.

Primary outcome-complete data for dose found the biggest increases were associated with previous treatment with a patient's current antipsychotic. This reflects use of an

antipsychotic with assumed previous efficacy but in larger doses given the likelihood of more severe symptoms in an acute subsequent episode (Taylor et al., 2015). A greater number of previous admissions and longer length of admission, both measures of severity and chronicity of illness, were also associated with higher doses. Interestingly women received lower doses than men possibly because of pharmacokinetic or weight differences (mean weight for females was 64.8kg vs. males 73.1kg) (Perry, 2001; Rummel-Kluge et al., 2010). Complete case data produced similar results but also included being sectioned under the Mental Health Act as a significant factor for a larger dose. This, like number and length of admissions, is a reflection of illness severity as those patients who are detained involuntarily often have more serious illness. Ethnicity was not associated with any significant differences in dose in both primary outcome-complete and complete case analyses.

High dose (more than 100% of BNF maximum dose) primary outcome-complete data found consultant psychiatrists of black ethnicity, compared with white, were more likely to prescribe high dose antipsychotics. Consultant psychiatrists of Chinese/other ethnicity were associated with high do117se prescribing in the complete case analysis. These associations were unexpected but after dissemination of findings of earlier studies on antipsychotics and ethnicity, ethnic minority prescribers reported informally that they were very surprised by the results. They said they purposely prescribed higher doses for black patients as they were more severely ill on admission to hospital. These comments have been explored further in a later study in Chapter 5. Having previously been treated with their current antipsychotic was associated with high doses in both analyses. Again, as with percentage maximum dose, high doses could be used when restarting a previously effective antipsychotic treatment in an acutely unwell inpatient.

Weight was associated with high doses in the complete case analysis as body size may affect prescribers' perception of a need for larger doses. This could of course be an incidental finding as many antipsychotics are commonly known to cause weight gain (Rummel-Kluge et al., 2010). Lower odds of high doses were associated in the complete case analysis with not having schizophrenia, possibly because antipsychotics are often used for psychiatric conditions where lower doses may be required e.g. in patients with autism or personality disorders (Barnard et al., 2002; Black et al., 2014).

As patients aged they were less likely to be prescribed more than one antipsychotic. This may reflect a greater severity of illness and/or a greater risk of violence in younger patients (Hodgins & Riaz, 2011; National Institute for Health and Care Excellence, 2015). Then again there have been concerns that young, black patients are perceived stereotypically as more violent than other ethnic groups possibly accounting for these results(Prins, 1993). Interestingly when data for all ethnicities (white, black, other) was analysed in Chapter 4, increasing age was associated with a greater risk of antipsychotic polypharmacy. Most polypharmacy occurs through 'when required or PRN' use of antipsychotics (Paton et al., 2008). When required antipsychotics are used for behavioural disturbance or rapid tranquillisation so may reflect a greater prevalence of this conduct in younger patients (National Institute for Health and Care Excellence, 2015). Polypharmacy could be a proxy measure of illness severity so it would be expected that being involuntarily detained would be associated with being prescribed more than one antipsychotic. Previous use of current treatment increased the odds of being administered more than one antipsychotic. This perhaps reflects a chronic or treatment-resistant illness course resulting in addition of further medication (Barnes & Paton, 2011). Use of intramuscular antipsychotics increased the risk of being on more

than one antipsychotic in the primary outcome-complete case analysis only. This could have been because patients switching to depot medication remained on oral treatment during the transfer. Co-prescription of depot with oral medication is commonplace despite the illogical nature of the combination (Barnes et al., 2009).

For polypharmacy administered complete case and primary outcome-complete case analyses produced similar results. As with polypharmacy prescribed, as patients aged they were less likely to be administered more than one antipsychotic. Again this may reflect illness severity or violence risk in younger patients. The odds of receiving more than one antipsychotic were greater in those who had completed secondary school compared with only primary. This association is difficult to explain as higher educational attainment usually predicts lower rates of psychotic symptomatology (Geddes et al., 1994). As such one would expect those who had received secondary level education, compared with primary, to have a lower risk of polypharmacy administered. Having a chronic illness, as reflected in number of previous admissions, was, unsurprisingly, associated with taking more than one antipsychotic. As with polypharmacy prescribed use of intramuscular antipsychotics and previous use of current treatment increased the risk of being administered more than one antipsychotic.

Factors associated with prescribing of a first generation type of antipsychotic were the same for both complete and primary outcome-complete case analyses. Anticholinergic medications are usually used with FGAs to treat EPSE so the association of not taking an anticholinergic and having a lower odds of being prescribed a FGA was as expected. However having a consultant psychiatrist of black ethnicity was associated with a lower odds of being prescribed an older antipsychotic. Again as with the association with

ethnic minority psychiatrist and high dose antipsychotic use, the relationship between prescriber ethnicity and antipsychotics is explored in a further study in Chapter 5. Most intramuscular forms of antipsychotics are available as depots. The odds of receiving a FGA were ten to twelvefold higher if receiving an intramuscular form. This is unsurprising as, at the time of data collection, there was only one SGA available as a depot formulation i.e. risperidone long-acting injection (British Medical Association and Royal Pharmaceutical Society of Great Britain, 2008). Short-acting injectable antipsychotics are usually used for rapid tranquillisation. The only short-acting SGA available at the time was olanzapine. This formulation is rarely prescribed (as reflected by results in Table 20) as it cannot be administered concurrently with lorazepam injection, an agent commonly used for behavioural disturbance (Datapharm Communications Ltd, 2016). Indeed olanzapine short-acting injection has since become unavailable in the UK.

Confounders associated with cost were the same for primary outcome-complete and compete case analyses. Antipsychotic costs were higher for those not taking an anticholinergic medication. SGAs are, in general, more expensive than FGAs (Monthly Index of Medical Specialities, December 2008) and anticholinergics are usually prescribed to treat extra-pyramidal adverse effects of the latter. Thus patients taking newer agents are less likely to be on an anticholinergic and so costs would be expected to be higher. Higher costs were associated with having had their current antipsychotic treatment before. Previous treatment with a patient's current antipsychotic and a longer length of admission were also associated with total dose so higher costs may reflect higher doses.

Route of administration was not an a priori outcome and post-hoc analysis found black patients were more likely than white to receive an antipsychotic via the intramuscular route. However a logistic regression analysis, controlling for all confounding factors, found ethnicity was not associated with route (see Chapter 4). Previous studies have found that black patients are more likely than white to have been prescribed a depot antipsychotic (Kreyenbuhl et al., 2003; Lloyd & Moodley, 1992; Shi, 2007; Woods et al., 2003). These studies did not control for multiple confounding factors and may account for the differing results.

2.4.4 WHICH ANTIPSYCHOTICS DID PRESCRIBERS USE?

As well as the six prescribing outcomes the individual antipsychotic choice of prescribers was examined. The most frequently prescribed antipsychotics were risperidone (oral and long-acting injection) and oral olanzapine. This pattern of antipsychotic prescribing replicates efficacy and effectiveness outcomes of randomised controlled trials and meta-analyses (Leucht et al., 2009; Lieberman et al., 2005) which consistently rank olanzapine and risperidone as the most effective agents in non treatment-resistant psychotic illness (Stroup et al., 2006). At the time of data collection, oral risperidone was available as a generic product at a reduced cost which is likely to have increased the frequency of prescribing. Conversely risperidone long-acting injection was the only SGA available as a long-acting formulation at the time of the data collection and, despite its high cost, was still the most frequently prescribed injectable preparation.

Clozapine use was not an a priori outcome and, unexpectedly, its use did not differ by ethnicity. Regular full blood count testing is mandatory when taking clozapine as it can

cause neutropenia and agranulocytosis. If levels of white cells fall below specified values then clozapine must be stopped. Black patients are more likely than white to develop neutropenia on clozapine so limiting its use in black people (Whiskey et al., 2011). A 'benign ethnic neutropenia' classification from a haematologist allows lower FBC parameters to be used for some black patients. These results may reflect an awareness and use of the BEN system thus allowing greater use of clozapine in black patients.

2.4.5 Comparison with previous studies

Most of the studies examining antipsychotic use by ethnicity have been completed in the US. Differences in antipsychotic treatment in black and white patients included; a greater likelihood of receiving an antipsychotic (Delbello et al., 2000; Flaskerud & Hu, 1992; Szarek & Goethe, 2003), higher doses (Diaz & De Leon, 2002; Segal et al., 1996), older drugs (Daumit et al., 2003; Fleck et al., 2002) and more frequent use of depot formulations (Kuno & Rothbard, 2002). These studies adjusted, unlike the present study, for only a few confounding factors affecting the prescribing of antipsychotics. Outcomes from these studies may not be comparable with ours because of differences in design and other factors related to healthcare settings and practices in different countries at different times.

There are few UK studies examining ethnicity and antipsychotic use. One survey (Lloyd & Moodley, 1992) found no significant differences (after adjustment for five confounding variables) in doses of antipsychotics taken by black and white patients. But black patients were more likely than white to be receiving a depot and at a significantly higher dose. The findings of this study differ from these earlier results, after adjustment

for confounders, for route of administration. Other UK studies, which were not designed to specifically examine prescribing by ethnicity, have not found an effect of ethnicity on antipsychotic high dose use (Paton et al., 2008) and polypharmacy (Lelliott, 2002). The earlier cross-sectional surveys of antipsychotic prescribing and ethnicity included several hundred patients from three NHS mental health trusts and again accounted for multiple confounding factors (Connolly et al., 2007; Connolly & Taylor, 2008). A recent study of antipsychotic use by ethnicity in a large, multicentre sample of community patients (Das-Munshi et al., 2018) found that black patients, compared with white, were more likely to be prescribed depot antipsychotics and were less likely to be prescribed clozapine. Mixed patients were more likely than white to receive high dose antipsychotic treatment. Overall the older surveys were undertaken on inpatients. They found few differences between black and white patients for the same outcomes used in this study although higher costs of antipsychotic medication and polypharmacy were significantly more likely in black patients. For full details of previous studies of antipsychotic prescribing and ethnicity see Chapter 1.

2.4.6 Limitations

Limitations of the study include the cross-sectional design, which allows examination of prescribing practice at only a single time point. This design is cost effective but cannot confirm causation. Other researchers have predominantly used survey study methods (see Appendix 3).

Black patients in the study included black British, black African, black Caribbean and black other groups whilst white patients included white British, white Irish and white other. Classification of ethnicity using the Office of National Statistics groups masked

the heterogeneity of the people in these categories and could have affected the results. For example prescribers may have used higher doses for the black Caribbean group but the effect was concealed by inclusion in a larger black patient group.

Not all data on confounding factors was obtainable for all patients. The total number of black and white patients in this analysis was 972. Primary outcome-complete data accounted for 938 (96.5%) cases with missing data imputed for incomplete variables. The primary outcome-complete and complete cases results have been included so these two methods of analysis can be compared. Overall there appeared to be few if any major differences between the data sets.

Centres were recruited for this study by approaching mental health trusts containing the largest populations of black and minority ethnic group patients. These centres, because of their ethnically diverse patient population, may be in some way more or less likely to demonstrate prejudicial prescribing (using higher doses, numbers, older types, injectable routes of antipsychotics to an individual member of or ethnic group because of a negative attitude or belief about that group) in a multicultural environment which may improve or worsen racial tolerance. Furthermore psychiatry is a medical speciality known for it racial diversity (Goldacre et al., 2004) which may, or may not, affect prejudice. Nonetheless, a previous study (Connolly & Taylor, 2008) included one centre, Oxleas that had a predominantly white population and did not find differences in antipsychotic prescribing between centres. Centre was not included as a potential confounder in this study because variation in prescribing by centre was considered to be an outcome rather than a confounder. A separate analysis including centre as a confounder did not alter results (see Chapter 3).

Confidence intervals around some outcome measures were wider than anticipated. This was a result of larger than expected variances and because of the large number of confounding variables identified and accounted for in the analysis. Many of the variables included in the models had several levels. This added to the complexity of the models and possibly poor model fit. The results could have been affected by the inclusion of too many variables i.e. the overadjustment of outcomes. Overadjustment is defined as "Statistical adjustment by an excessive number of variables or parameters, uninformed by substantive knowledge (e.g. lacking coherence with biologic, clinical, epidemiological, or social knowledge). It can obscure a true effect or create an apparent effect when none exists.(Breslow, 1982)" Overadjustment may bias results towards the null hypothesis. Confounders were determined by examining previous research and seeking expert advice from professionals working in the field of ethnicity research. All confounders collected were included in the models as described – many more than in previous studies (see Appendix 2) – which may have had an impact on the results. Variables could have been limited more carefully to avoid possible overadjustment. Unadjusted results are available for each outcome (see Figures 5 to 9 and 12) with prescribed polypharmacy and use of an FGA more likely in black patients. Interestingly these results differ markedly from the adjusted outcomes.

All of these limitations may have resulted in the negative findings. This study analysed data from black and white patients only as concerns about differences in prescribing by ethnicity have focussed mostly on the difference between these two groups. Furthermore these were the two largest ethnic groups in UK inpatient mental health services and in my sample. This study did not analyse the effect of each centre on the

outcomes. The next chapter will investigate differences in prescribing by individual centres and also total data including centre as a confounding variable.

2.5 CONCLUSIONS

There have long been concerns expressed by patients, carers (Norfolk Suffolk & Cambridgeshire Strategic Health Authority, 2003; South London and Maudsley NHS Trust, 2005) and the UK government (Department of Health, 2003) about differences in prescribing of antipsychotics by ethnicity. This study addresses these concerns and, notwithstanding the limitations described above, the adjusted findings suggest that across eight NHS trusts prescribing of antipsychotics for six major outcomes is not different for black and white patients. Unadjusted findings found prescribed polypharmacy and use of FGA were more likely in black patients. The significant limitations of the study may have resulted in negative findings.

CHAPTER 3 ANTIPSYCHOTIC PRESCRIBING BY ETHNICITY - CENTRE ANALYSIS

3.1 INTRODUCTION

Antipsychotic prescribing may be influenced by ethnicity. Specifically black patients, compared with white, are reported to be more likely to receive higher doses, older antipsychotic treatments and more than one antipsychotic. The studies reporting these differences have been predominantly from the US although earlier multicentre UK studies have, overall, not reported major differences in antipsychotic prescribing (Connolly et al., 2007; Connolly & Taylor, 2008). An in-depth review of antipsychotic prescribing by ethnicity is described in Chapter 1 with further details provided in Appendices 3 and 4.

A previous UK study of antipsychotic prescribing in black and white inpatients in three London NHS trusts found that centre effects were a significant predictor of polypharmacy (Connolly & Taylor, 2008). One of the three centres had extremely high levels of polypharmacy for black compared with white patients (74% vs. 37% - other centres 13% vs. 17% and 16% vs. 10% respectively). This shows the importance of analysis by centre to determine if irregular prescribing by any centres is influencing the overall result. Such sub-analysis also provides individual centres with data to enable them to take the necessary steps to improve prescribing practice if required.

Nationally, POMH-UK was created to help NHS trusts improve their prescribing in psychiatry. It has audited numerous areas of prescribing practice, for example antipsychotic high doses and polypharmacy, collecting data from over 3000 patients in

32 services in a baseline then a re-audit 1-year later. Unfortunately the re-audit found little change in these prescribing outcomes (Paton et al., 2008). POMH-UK publishes results and NHS trusts are benchmarked anonymously against each other in an effort to improve prescribing. It has also undertaken quality improvement programmes to help implement their work and encourage prescribers to change poor prescribing habits. These programmes have, overall, had modest success (Paton et al., 2008; Thompson et al., 2008) but some centres have made dramatic improvements with sustained and concerted efforts over many years (Mace & Taylor, 2015).

The study in Chapter 1 did not analyse the effect of each centre on outcomes. Individual centres i.e. NHS mental health trusts may have different prescribing practices that require analysis. This chapter reports the individual centre results for each outcome from a multicentre cross-sectional survey of antipsychotic prescribing in black and white patients. It also reports primary outcome-complete total data analysis for black and white patients when centre was included as a variable. Centre effects (SLaM vs. non-SLaM) for all ethnicities and outcomes (including route of administration and clozapine use) are reported separately in Chapter 4.

3.2 METHOD

In summary, eight UK centres (six NHS trusts in London, one in Nottingham and one in Manchester) completed data collection during late 2008 and early 2009. These centres were included because they served the highest proportion of black and minority ethnic groups in the UK. Ethnicity classification was categorised according to the Office for National Statistics groupings (see Chapter 2). The main outcomes of the study were dose, high dose, polypharmacy (prescribed or administered), type of antipsychotic and cost.

Over twenty potential confounders were identified from previous studies (see Appendix 2) and expert opinion. The confounders were defined for the data collectors as in Appendix 10. Data were collected from casenotes and prescription charts by pharmacists or medical staff. Subjects included were all inpatients on acute adult wards prescribed a regular antipsychotic or having received an as required dose in the previous 24 hours.

The study compared the six outcomes previously described (in Chapter 2) between two groups (black and white patients) and linear and logistic regression analysis was used to adjust the resulting comparisons for the effect of confounding variables. Baseline demographic and clinical characteristics were analysed by ethnicity.

Details of the method and statistical analysis have been fully described in Chapter 2.

3.3 RESULTS

Data were collected for 938 patients from eight centres of which 541 (57.7%) were white and 397 (42.3%) black. All centre results were anonymised and individual centres were notified of their number code. Demographic and clinical characteristics of these patients by ethnicity and centre are listed in Chapter 2. Not all confounder data were available for all subjects at the time of the survey as described in the previous chapter. Primary outcome (i.e. total dose) complete data were used with multiple imputations for missing data for both the individual centre analyses and total data analysis with centre for black and white patients. Each outcome model was adjusted for multiple confounders as described below (see Tables 21 to 26). Centre data for black and white ethnicity were analysed separately so the effect of individual centres could be assessed. For primary

outcome-complete total data analysis for black and white ethnicities centre was included as a confounder in this chapter.

Note that all results compare black with white patients i.e. white is the reference category. A negative effect size/adjusted percentage difference or an odds ratio less than 1 means black patients are less likely than whites to have this outcome.

3.3.1 Individual Centre Analyses

Statistically significant results for the outcome of median dose were as follows. In centre 2 black patients were prescribed a 13% lower median dose of antipsychotic than whites (adjusted percentage difference = -13.08%, 95% confidence intervals -25.71, -0.45, p=0.04). Whilst in centre 7 black patients were prescribed an almost 81% higher median dose of antipsychotic than whites (adjusted percentage difference = 80.87, 95% CI 50.51, 111.23, p <0.001).

Statistically significant results for the outcome of median cost were as follows. In centres 6 and 7 black patients antipsychotic treatment cost more than whites (centre 6 adjusted cost difference = £31.13, 95% CI 2.82, 59.43, p=0.03; centre 7 adjusted cost difference = £95.06, 95% CI 35.37, 154.76, p=0.003).

Statistically significant results for outcome of high dose (> 100% BNF maximum dose) were as follows. No centres had a significant difference after adjustment for confounders. For the unadjusted results, centre 7 black patients were more likely than whites to receive a high dose (*unadjusted* OR = 3.87, 95% CI 1.24, 12.14, p=0.02).

Statistically significant results for polypharmacy prescribed were as follows. No centres had a significant difference after adjustment for confounders. For the unadjusted results, centre 7 black patients were more likely than whites to be prescribed more than one antipsychotic (*unadjusted* OR = 2.85, 95% CI 1.09, 7.45, p=0.03).

Statistically significant results for administered polypharmacy were as follows.
No centres had a significant difference after adjustment for confounders. For the unadjusted results, centre 7 black patients were more likely than whites to receive more than one antipsychotic (*unadjusted* OR 3.5, 95% CI 1.36, 9.02, p=0.01).

Statistically significant results for type of antipsychotic were as follows. Centre 3 black patients were significantly more likely than whites to receive FGA (adjusted OR = 4.44, 95% CI 1.22, 16.14, p=0.02).

Full results are displayed in Tables 21 through to 26.

TABLE 21 INDIVIDUAL CENTRE RESULTS BY ETHNICITY FOR MEDIAN DOSE

Centre Number	Number of patients (1^0 outcome complete)	Unadjusted effect size/percentage difference (95% CI)	P	Number of patients (complete cases)	Adjusted effect size/percentage difference (95% CI)	p	Outcome adjusted for following confounders
1	199	-6.97 (-18.31, 4.38)	0.23	198	-7.67 (-18.23, 2.89)	0.15	Previous admissions; gender; duration of illness; length of treatment; previous treatment with current antipsychotic
2	109	-11.94 (-24.53, 0.65)	0.06	102	-13.08 (-25.71, -0.45)	0.04	Previous treatment with current antipsychotic; route
3	98	3.49 (-12.68, 19.66)	0.67	93	0.46 (-15.37, 16.29)	0.95	Smoking status; section status; weight
4	80	25.16 (0.63, 49.69)	0.05	78	16.89 (-5.15, 38.94)	0.13	Substance misuse; section status; employment; previous treatment with current antipsychotic; smoking status
5	121	-3.25 (-19.70, 13.20)	0.70	114	-13.65 (-29.48, 2.19)	0.09	Weight; length of admission
6	148	6.46 (-6.32, 19.23)	0.32	106	6.60 (-7.72, 20.91)	0.36	Previous treatment with current antipsychotic; length of admission
7	94	35.17 (16.28, 54.06)	<0.001	34	80.87 (50.51, 111.23)	<0.001	Previous admissions; weight; length of admission
8	89	10.75 (-15.47, 36.96)	0.42	Not possible to calculate adjusted effect size			

TABLE 22 INDIVIDUAL CENTRE RESULTS BY ETHNICITY FOR MEDIAN COST (£)

Centre Number	Number of patients (1^0 outcome complete)	Unadjusted effect size (95% CI)	p	Number of patients (complete cases)	Adjusted effect size (95% CI)	p	Outcome adjusted for following confounders
1	199	-9.30 (-32.48, 13.88)	0.43	198	-5.77 (-28.17, 16.63)	0.61	Length of treatment; previous treatment with current antipsychotic; weight; anticholinergic use
2	109	-9.68 (-37.66, 18.30)	0.49	102	-10.67 (-39.56, 18.22)	0.47	Previous treatment with current antipsychotic
3	98	4.14 (-33.52, 41.82)	0.83	93	2.90 (-30.76, 36.57)	0.86	Length of admission; smoking status; weight; route; length of treatment
4	80	17.24 (-41.25, 75.72)	0.56	78	-16.70 (-71.00, 37.60)	0.54	Substance misuse; compliance history
5	121	-17.69 (-55.42, 20.04)	0.36	114	-21.95 (-59.59, 15.69)	0.25	Length of admission; length of treatment
6	148	11.80 (-15.48, 39.09)	0.39	106	31.13 (2.82, 59.43)	0.03	Length of admission; route; previous admissions; duration of illness; employment status; anticholinergic use
7	94	59.81 (19.09, 100.54)	0.004	34	95.06 (35.37, 154.76)	0.003	Previous admissions; substance misuse
8	89	29.21 (-28.36, 86.77)	0.32	Not possible to calculate adjusted effect size			

TABLE 23 INDIVIDUAL CENTRE RESULTS BY ETHNICITY FOR HIGH DOSE (> 100% BNF MAXIMUM)

Centre Number	**Number of patients (1^0 outcome complete)**	**Unadjusted OR (95% CI)**	**p**	**Number of patients (complete cases)**	**Adjusted OR (95% CI)**	**P**	**Outcome adjusted for following confounders**
1	199	0.84 (0.36, 1.95)	0.68	192	0.75 (0.30, 1.85)	0.53	Previous treatment with current antipsychotic; gender; previous admissions; smoking status; ethnicity of consultant
2	109	0. 21 (0.02, 1.91)	0.16	Not possible to calculate adjusted odds ratio			
3	98	0.73 (0.20, 2.61)	0.63	43	0.13 (0.02, 1.03)	0.05	Route; weight
4	80	1.67 (0.30, 9.27)	0.56	Not possible to calculate adjusted odds ratio			
5	121	1.55 (0.46, 5.28)	0.48	93	1.51 (0.36, 6.37)	0.57	Weight
6	148	1.36 (0.40, 4.69)	0.62	43	1.50 (0.32, 7.01)	0.61	None
7	94	3.87 (1.24, 12.14)	0.02	Not possible to calculate adjusted odds ratio			
8	89	1.17 (0.29, 4.76)	0.82				

TABLE 24 INDIVIDUAL CENTRE RESULTS BY ETHNICITY FOR POLYPHARMACY PRESCRIBED

Centre Number	Number of patients (1^0 outcome complete)	Unadjusted OR (95% CI)	p	Number of patients (complete cases)	Adjusted OR (95% CI)	P	Outcome adjusted for following confounders
1	199	1.56 (0.85, 2.87)	0.15	198	1.49 (0.80, 2.78)	0.21	Previous treatment with current antipsychotic; compliance history
2	109	0.94 (0.44, 2.01)	0.88	101	0.72 (0.31, 1.69)	0.45	Anticholinergic use; gender
3	98	1.06 (0.46, 2.46)	0.89	90	0.68 (0.22, 2.05)	0.49	Section status; age; smoking status; weight
4	80	4.4 (1.12, 17.24)	0.03	78	4.11 (0.99, 17.01)	0.05	Substance misuse
5	121	1.45 (0.67, 3.14)	0.34	108	1.34 (0.54, 3.34)	0.53	Previous treatment with current antipsychotic; weight; anticholinergic use
6	148	2.38 (1.19, 4.76)	0.02	101	1.75 (0.70, 4.41)	0.23	Ethnicity of consultant; previous treatment with current antipsychotic; compliance history; anticholinergic use
7	94	2.85 (1.09, 7.45)	0.03	Not possible to calculate adjusted odds ratio			
8	89	2.26 (0.74, 6.88)	0.15				

TABLE 25 INDIVIDUAL CENTRE RESULTS BY ETHNICITY FOR POLYPHARMACY ADMINISTERED

Centre Number	**Number of patients (1^0 outcome complete)**	**Unadjusted OR (95% CI)**	**p**	**Number of patients (compete cases)**	**Adjusted OR (95% CI)**	**P**	**Outcome adjusted for following confounders**
1	199	1.18 (0.58, 2.39)	0.65	192	1.20 (0.57, 2.52)	0.63	Previous treatment with current antipsychotic; anticholinergic use; smoking status
2	109	0.97 (0.36, 2.62)	0.96	96	1.31 (0.45, 3.82)	0.62	Route
3	98	1.10 (0.45, 2.66)	0.84	90	0.43 (0.13, 1.38)	0.16	Previous treatment with current antipsychotic; age; route
4	80	1.36 (0.37, 4.96)	0.64	73	2.70 (0.44, 16.36)	0.28	Length of treatment; previous admissions; gender; anticholinergic use
5	121	1.87 (0.68, 5.17)	0.23	108	1.39 (0.40, 4.83)	0.61	Weight; anticholinergic use; previous treatment with current antipsychotic
6	148	1.47 (0.62, 3.45)	0.38	101	1.06 (0.35, 3.23)	0.92	Language
7	94	3.5 (1.36, 9.02)	0.01	Not possible to calculate adjusted odds ratio			
8	89	1.29 (0.40, 4.20)	0.67				

TABLE 26 INDIVIDUAL CENTRE RESULTS BY ETHNICITY FOR FIRST GENERATION ANTIPSYCHOTIC USE

Centre Number	Number of patients (1^0 outcome complete)	Unadjusted OR (95% CI)	p	Number of patients (complete cases)	Adjusted OR (95% CI)	P	Outcome adjusted for following confounders
1	199	1.38 (0.69, 2.76)	0.37	172	0.81 (0.28, 2.34)	0.70	Route; anticholinergic use; duration of illness; section status
2	109	1.07 (0.48, 2.39)	0.88	98	1.59 (0.52, 4.85)	0.42	Route; anticholinergic use; ethnicity of consultant; compliance history
3	98	2.47 (0.92, 6.60)	0.07	90	4.44 (1.22, 16.14)	0.02	Route; previous admissions; section status
4	80	1.5 (0.46, 4.86)	0.50	76	1.99 (0.39, 10.09)	0.41	Route; substance misuse; smoking status; duration of illness
5	121	3.17 (1.25, 8.04)	0.02	113	2.06 (0.57, 7.40)	0.27	Anticholinergic use; route; previous treatment with current antipsychotic; language; substance misuse
6	148	1.40 (0.63, 3.12)	0.41	88	0.18 (0.03, 1.01)	0.05	Route; length of treatment; previous admissions; weight
7	94	0.77 (0.25, 2.38)	0.66	Not possible to calculate adjusted odds ratio			
8	89	0.97 (0.24, 3.88)	0.97				

3.3.2 PRIMARY OUTCOME-COMPLETE DATA ANALYSIS WITH CENTRE

TABLE 27 LINEAR REGRESSION MODEL FOR MEDIAN TOTAL PERCENTAGE MAXIMUM DOSE WITH CENTRE (PRIMARY OUTCOME-COMPLETE, N=938)

Variable	**Coefficient**	**Standard Error**	**p value**	**95% CI**
Ethnicity: black	2.34	2.71	0.39	-2.98, 7.67
Length of admission (log)	4.78	0.97	<0.01	2.87, 6.68
Centre 2	-6.71	4.03	0.10	-14.62, 1.19
Centre 8	7.92	4.62	0.09	-1.15, 16.99
Centre 7	7.42	4.48	0.10	-1.37, 16.20
Gender: female	-8.26	2.78	<0.01	-13.71, -2.80
Previous admissions: more than 5	3.40	1.51	0.03	0.42, 6.37
Previous treatment with current antipsychotic: yes	12.63	3.04	<0.01	6.62, 18.63
Route: intramuscular	-2.93	3.09	0.34	-9.00, 3.13
Legal status: sectioned	6.22	2.90	0.03	0.53, 11.90
Weight 1	0.19	0.34	0.58	-0.50, 0.87
Weight 2	1.07	1.12	0.35	-1.18, 3.31
Weight 3	-5.51	3.81	0.15	-13.11, 2.08

Higher doses were associated with a longer length of admission (log), a greater number of previous admissions, previous treatment with current antipsychotic and being sectioned under the Mental Health Act. Lower doses were associated with female gender. Centre and ethnicity effects were not significantly associated with dose. The weight variable violated an assumption of linear regression that there must be a linear relationship between outcome and confounder. It was transformed and included in the model using restricted cubic splines (a third order polynomial equation) using four knots (where polynomial sections join) equally spaced.

TABLE 28 LOGISTIC REGRESSION MODEL FOR HIGH DOSE WITH CENTRE (PRIMARY OUTCOME-COMPLETE, N=938)

Variable	**Odds Ratio (OR)**	**Standard Error**	**p value**	**95% CI**
Ethnicity: black	1.08	0.25	0.75	0.68, 1.70
Centre 2	0.39	0.19	0.05	0.15, 1.01
Centre 8	1.44	0.49	0.29	0.73, 2.82
Centre 7	1.58	0.53	0.18	0.81, 3.07
Diagnosis: not schizophrenia	0.55	0.19	0.09	0.28, 1.11
Education: A level/up to age 18	0.53	0.17	0.05	0.28, 1.00
Previous treatment with current antipsychotic: yes	2.66	0.80	<0.01	1.46, 4.83
Ethnicity of consultant: Chinese/other	2.01	0.50	0.01	1.23, 3.29
Legal status: sectioned	1.17	0.30	0.55	0.71, 1.92
Weight (kg)*	1.01	0.01	0.03	1.01, 1.02

*OR for 1kg weight change

High doses were associated with having previously been treated with the current antipsychotic, having a consultant of Chinese/other ethnicity and a heavier weight.

TABLE 29 LOGISTIC REGRESSION MODEL FOR POLYPHARMACY PRESCRIBED WITH CENTRE (PRIMARY OUTCOME-COMPLETE CASES, N=938)

Variable	**Odds Ratio (OR)**	**Standard Error**	**p value**	**95% CI**
Ethnicity: black	1.35	0.21	0.05	1.00, 1.83
Age (years)*	0.98	0.01	<0.01	0.97, 0.99
Centre 2	2.40	0.56	<0.01	1.52, 3.78
Centre 3	3.91	0.99	<0.01	2.38, 6.41
Centre 5	1.39	0.32	0.15	0.89, 2.20
Centre 8	2.06	0.53	<0.01	1.24, 3.42
Centre 7	2.75	0.70	<0.01	1.66, 4.53
Centre 4	2.46	0.65	<0.01	1.46, 4.14
Previous treatment with current antipsychotic: yes	1.79	0.27	<0.01	1.33, 2.41
Ethnicity of consultant: black	1.24	0.27	0.34	0.80, 1.90
Route: intramuscular	1.53	0.25	0.01	1.11, 2.11
Legal status: sectioned	1.63	0.26	<0.01	1.19, 2.23
Employment: student	0.40	0.20	0.07	0.15, 1.107

*OR for change per increase in years,

Polypharmacy prescribed was associated with younger age (as each year increase in age reduced the odds of being prescribed polypharmacy by 2%), being a patient at centres 2, 3, 4, 7 and 8, having previously been treated with current antipsychotic, intramuscular route of administration and being sectioned under the Mental Health Act.

TABLE 30 LOGISTIC REGRESSION MODEL FOR POLYPHARMACY ADMINISTERED WITH CENTRE (PRIMARY OUTCOME-COMPLETE CASES, N=938)

Variable	**Odds Ratio (OR)**	**Standard Error**	**p value**	**95% CI**
Ethnicity: black	1.13	0.20	0.48	0.80, 1.60
Age (years)*	0.98	0.01	<0.01	0.96, 0.99
Centre 3	1.84	0.47	0.02	1.11, 3.04
Centre 8	1.70	0.48	0.06	0.98, 2.95
Centre 7	2.47	0.65	<0.01	1.47, 4.14
Education: secondary	1.61	0.28	<0.01	1.14, 2.28
Previous admissions: more than 5	1.31	0.14	0.02	1.05, 1.63
Previous treatment with current antipsychotic: yes	2.04	0.47	<0.01	1.29, 3.23
Route: intramuscular	1.80	0.33	<0.01	1.26, 2.58
Legal status: sectioned	1.31	0.26	0.16	0.89, 1.93

*OR for change per increase in years

Polypharmacy administered was associated with being a patient at centres 3 and 7, having been educated to secondary level, having a greater number of previous admissions, previously being treated with current antipsychotic and IM route of administration. Antipsychotic monotherapy was associated with younger age (each year increase in age reduced the odds of being administered polypharmacy by 2%).

TABLE 31 LOGISTIC REGRESSION MODEL FOR FIRST GENERATION TYPE OF ANTIPSYCHOTIC WITH CENTRE (PRIMARY OUTCOME-COMPLETE CASES, N=938)

Variable	**Odds Ratio (OR)**	**Standard Error**	**p value**	**95% CI**
Ethnicity: black	1.31	0.25	0.15	0.91, 1.91
Anticholinergic use: no	0.23	0.05	<0.01	0.15, 0.35
Centre 2	1.96	0.54	0.01	1.14, 3.36
Centre 6	0.71	0.19	0.21	0.41, 1.21
Centre 4	2.46	0.77	<0.01	1.33, 4.55
Previous treatment with current antipsychotic: yes	1.31	0.26	0.19	0.88, 1.95
Ethnicity of consultant: black	0.53	0.17	0.04	0.28, 0.98
Route: intramuscular	11.38	2.19	<0.01	7.80, 16.59
Length of treatment (days)	1.03	0.02	0.07	0.99, 1.07

FGA use was associated with being a patient at centres 2 and 4 and IM route of administration of an antipsychotic. Having a consultant of black ethnicity and not using an anticholinergic were associated with reduced odds of having a FGA.

TABLE 32 LINEAR REGRESSION MODEL FOR MEDIAN COST WITH CENTRE (PRIMARY OUTCOME-COMPLETE N=938)

Variable	**Coefficient**	**Standard Error**	**p value**	**95% CI**
Ethnicity: black	3.01	5.88	0.61	-8.54, 14.56
Length of admission (log)	9.51	2.15	<0.01	5.28, 13.74
Anticholinergic use: no	25.91	7.82	<0.01	10.56, 41.27
Centre 2	-25.24	8.93	<0.01	-42.76, -7.72
Previous admissions: more than 5	6.41	3.32	0.05	-0.11, 12.93
Previous treatment with current antipsychotic: yes	17.05	6.68	<0.01	3.90, 30.21
Weight 1	0.06	0.72	0.93	-1.37, 1.49
Weight 2	2.89	2.31	0.21	-1.66, 7.45
Weight 3	-13.95	7.87	0.08	-29.43, 1.53

Higher costs of antipsychotic treatment were associated with a longer length of admission, not using anticholinergic medication and previously being treated with current antipsychotic. Being a patient at centre 2 was associated with lower costs of

antipsychotic treatment. As with the dose outcome, some variables violated an assumption of linear regression that there must be a linear relationship between outcome and confounder. These were transformed and included in the model using the log scale for the length of admission in days and restricted cubic splines (a third order polynomial equation) using four knots (where polynomial sections join) equally spaced for the weight variable.

3.4 DISCUSSION

3.4.1 MAIN FINDINGS

There were several statistically significant differences between individual centres in prescribing for black and white patients when individual centre data were analysed separately. Specifically black patients were more likely than whites to receive higher median doses (centre 7), high doses (centre 7, unadjusted outcome), to be prescribed polypharmacy (centre 7, unadjusted outcome), to be administered polypharmacy (centre 7, unadjusted outcome) and to be prescribed a FGA (centre 3). Conversely at some centres black patients, compared with whites, received lower median doses (centre 2) and higher cost drug treatment (centres 6 and 7). Centre number 7 had worse prescribing outcomes for black patients compared with whites for four out of the six outcomes. This is a concern as these results may suggest racist prescribing in this centre – an effect that was largely masked when centre results were combined. Still it is important to note that for several of these outcomes it was not possible to adjust results for potential confounders because of small sample sizes. Centre 7 had the smallest sample size and was one of the centres with the largest proportion of missing data.

Each centre was informed of their results, highlighting differences, through a presentation and a written report. They were encouraged to investigate reasons for differences and to take remedial action where necessary.

As it was not possible to adjust all individual centres outcomes for confounders because of sample size constraints, it was important to analyse total black and white data including centre as a confounder. Primary outcome-complete data were analysed in detail in Chapter 2 without centre effects but when centre was included it was a significant predictor of several outcomes. In this analysis patients were more likely to be prescribed more than one antipsychotic in centres 2,3,4,7 and 8 and administered more than one antipsychotic in centres 3 and 7. Being prescribed more than one antipsychotic occurred in more centres than being administered more than one antipsychotic, in all likelihood because of PRN prescribing for behavioural disturbance (Paton et al., 2008). Those patients in centres 2 and 4 were more likely to receive a FGA. Restrictive formularies and funding, prescribing cultures or differing patient populations are potential causes. Centre 2 had lower costs of antipsychotic treatment possibly been because of greater use of cheaper FGA. For further discussion of the other variables associated with outcomes see section 2.4.3 and 4.4.1.

3.4.2 Comparison with Other Studies

Previous (mainly US) studies have found differences in antipsychotic prescribing between black and white patients (see Appendices 3 and 4). UK studies have, overall, not found such differences in inpatients (Connolly et al., 2007; Connolly & Taylor, 2008) but have done so in a large study of community patients {Das-Munshi, 2018 #1105. Indeed analysis of patients recruited in the study revealed no important

statistically significant differences in prescribing of antipsychotics between black and white patients after adjustment for confounding variables (see Chapter 2). Nevertheless individual centre differences can be masked in a combined data analysis as shown by the results in this chapter. Indeed a previous study found that polypharmacy rates were driven by one centre's data (Connolly & Taylor, 2008). National differences in prescribing by centre are highlighted by POMH-UK audits but NHS trusts are not compelled to be members of this organisation and significant costs and workloads are involved. Benchmarking data against other NHS trusts performance has resulted in those with poorer results making concerted efforts to change the culture and quality of prescribing, for example a reduction in high dose antipsychotic use from 58% to 10% and polypharmacy from 57% to 16% (Mace & Taylor, 2015).

Comparison of this analysis (primary outcome-complete, black and white patients with centre variable) with that in Chapter 2 (primary outcome-complete, black and white patients without centre variable) found variables associated with the outcomes were, overall, broadly similar. Furthermore in this analysis individual centres were significantly associated with several outcomes. Lower costs of antipsychotic treatment at centre 2 may have been related to their higher use of FGAs. Conversely higher costs were not associated with centres 3 and 7 even though polypharmacy administered was significantly more likely in these centres. Centre was a common association with polypharmacy prescribed - more likely in five centres (see Chapter 4 for further analyses). Unsurprisingly centres where polypharmacy prescribed was more likely had a greater risk of polypharmacy administered. Likewise higher use of FGAs through PRN prescribing may have contributed to centre 4's greater risk of polypharmacy prescribed. Reasons for these differences required follow-up by the centre involved.

3.4.3 LIMITATIONS

The study was not powered to detect differences between black and white patients in individual centres. Where differences were not shown it should not be assumed that there were none as confidence intervals were wide for all of the outcomes so limiting the accuracy of the results. Small sample sizes and missing confounder data meant that it was not possible to adjust all outcomes for all centres.

Multilevel modelling would have been a useful statistical technique to use on this data as the cases are nested at each centre. The analysis in section 3.3.2 with centre as a variable provides a preliminary analysis. Several centres had significant effects on the outcomes indicating clustering of effect.

Many of the variables included in the models had several levels. This added to the complexity of the models and possibly accounted for poor model fit. Inclusion of all variables collected in the study may have resulted in overadjustment of outcomes and bias towards the null hypothesis (see Section 2.4.6 for more details). Unadjusted results were available for the individual centre analyses and, where outcomes could be adjusted, some results differed. Specifically black patients were more likely to experience prescribed polypharmacy (centre 4 and centre 6) and FGA use (centre 5) when unadjusted (but not adjusted) data outcomes were examined. For some outcomes only unadjusted data were available; in centre 7 black patients were more likely than white to be prescribed high doses, administered and prescribed polypharmacy and have a higher cost of antipsychotic treatment. Conversely some insignificant unadjusted outcomes were significant when adjusted – in centre 2 median dose was higher for

black patients compared with white and for centre 3 FGA use greater for black compared with white patients.

Unfortunately this study was not funded to allow follow-up investigation with each centre to determine reasons for differences in prescribing. This would be a valuable future research project.

As in Chapter 2 classification of ethnicity using the Office of National Statistics groups masked the heterogeneity of the people in these categories and could have affected the results. Thus far the studies in this thesis have investigated the prescribing of antipsychotics in black and white patients only. Although Asian, mixed, Chinese/other patients are a smaller proportion of the UK inpatient mental health population, differences in the care of these groups has been reported (Care Quality Commission, 2010) and analysis of prescribing of antipsychotics for these populations is required. The next chapter analyses antipsychotic prescribing data from patients of all ethnicities to determine if there are any differences in outcomes.

3.5 CONCLUSIONS

It is difficult to reach firm conclusions on the centre analysis data despite significant results for some centres in both adjusted and unadjusted analyses. This is because of the limitations described earlier in Section 3.4.3. Even after accounting for these shortcomings, it is clear that for some centres, particularly centre 7, major differences in antipsychotic prescribing were recorded between black and white patients. Determination of the reasons for these disparities, however complex, requires further investigation and remedial action from the trusts identified in this report.

CHAPTER 4 PREDICTORS OF PRESCRIBING OUTCOMES AND ETHNICITY

4.1 INTRODUCTION

Poor prescribing of antipsychotics is common both nationally and worldwide and is not restricted to those from minority ethnic groups (Barnes & Paton, 2011). The prescribing measures most often employed are dose, high dose (either more than 100% of the BNF maximum percentage dose (i.e. dose divided by maximum licensed dose multiplied by 100) or more than 1g of CPZe) and combinations of antipsychotics (Harrington et al., 2002; Taylor et al., 2002). High doses often result from antipsychotic combinations (where the percentage maximum of each drug added together equals more than 100%) whether used inadvertently because of PRN use or deliberately by use of two or more regular antipsychotics.

Combining antipsychotic is, in most instances, not logical. This is because antipsychotics, unlike other groups of medicines for HIV or tuberculosis, have broadly similar mechanisms of action (Kapur & Seeman, 2001). Irrational and harmful antipsychotic combinations are numerous and the potential consequences are described in Table 33. The commonest combinations involve depots with oral antipsychotics, quetiapine with other antipsychotics and FGAs as PRNs (Taylor et al., 2015).

TABLE 33 RISKS ASSOCIATED WITH THE USE OF ANTIPSYCHOTIC COMBINATIONS

Antipsychotic Combination	**Risks**
Depot and oral	Defeats the purpose of ensuring compliance with an injection.
	Increased non-adherence (Fenton et al., 1997).
FGA and SGA	Financially costly.
	Exposes patients to metabolic, cardiac and movement side effects of both types of antipsychotic (Carnahan et al., 2006; Correll et al., 2007; Haddad, 2005; Haddad & Wieck, 2004; Peveler et al., 2008).
	Increased mortality (Joukamaa et al., 2006; Waddington et al., 1998).
Two FGAs	Increased risk of additive neurocognitive and cardiac effects (Carnahan et al., 2006; Elie et al., 2010).
	Greater mortality (Joukamaa et al., 2006).
Regular and PRN antipsychotic	Routinely used for inpatients for behavioural disturbance (National Institute for Health and Care Excellence, 2015).
	Lack of regular review of need may result in inadvertent high dose prescribing (Paton et al., 2008).

There appear to be clear differences in high dose antipsychotic prescribing and use of antipsychotic combinations for hospital inpatients compared with community patients. Lower rates of combinations are reported for those no longer in hospital (15% vs. approximately 40% in community (Patel et al., 2014; Paton et al., 2008)). This reflects differing patient characteristics (e.g. illness severity and chronicity, treatment resistance, diagnosis) in each treatment setting and one assumes the effects of routine PRN prescribing of antipsychotics for inpatients.

High dose antipsychotic prescribing is an indicator of poor prescribing quality and prescribing of combinations of antipsychotics is a major predictor of high doses (Paton et al., 2008). Again as with combinations of antipsychotics, high doses occur more frequently in inpatients (approximately a third of patients) than in community patients (in approximately a tenth) (Patel et al., 2014; Paton et al., 2008), probably because of

PRN prescribing. Studies of antipsychotic dose response have found that optimally effective doses are often found in doses at the lower end of the range e.g. risperidone 4mg (Ezewuzie & Taylor, 2006), aripiprazole 10-15mg (Sparshatt et al., 2010) and, given that antipsychotics have similar mechanisms of action, continuing to increase dopamine blockade does not have a beneficial effect for most patients.

Although there are some studies reporting the efficacy of high doses, many of these studies are dated, poorly designed and use mega-doses of antipsychotics e.g. 10g chlorpromazine equivalent doses (Taylor et al., 2015). Using high doses of SGAs such as quetiapine or olanzapine may yield modest benefits for some patients with treatment-resistant illness but data are conflicting (Boggs et al., 2008; Honer et al., 2012; Meltzer et al., 2008). Interestingly the seminal study of clozapine use in treatment-resistant schizophrenia compared clozapine with high dose chlorpromazine (doses up to 1800mg/day) treatment and found response rates of 30% and 4% respectively (Kane et al., 1988). Use of clozapine is, for most patients, a more successful treatment.

So why do prescribers continue to use antipsychotics in this way? There are a number of reasons why prescribing more than one antipsychotic may occur. It may be the result of a partial response to the first treatment (reflecting the inefficacy and lack of truly new pharmacological treatments for schizophrenia) (Harrington et al., 2002) or the prescriber may be using two antipsychotics together to avoid high doses of a single agent (but addition of BNF percentage maximum doses of each agent often results in high dose) or a PRN antipsychotic prescribing strategy for behavioural disturbance (Paton et al., 2008). A survey of US psychiatrists found a third would add a second antipsychotic if a patient did not respond to the first (Kreyenbuhl et al., 2007a) whilst

two thirds of psychiatrists in Denmark would rather prescribe two antipsychotics than clozapine (Nielsen et al., 2010). Prescribing combinations of antipsychotics is clearly entrenched practice in some countries but psychiatrists are aware such practices are ineffective (Kreyenbuhl et al., 2007a).

There are situations where prescribing antipsychotics in combination is necessary or advantageous. These include switching between antipsychotics (although this can be a situation where patients become erroneously 'stuck' on two agents if the first is not withdrawn as planned (Taylor, 1997)); augmentation of clozapine to improve efficacy (unfortunately only small improvements have been found (Taylor & Smith, 2009)); managing side effects of an effective antipsychotic (e.g. aripiprazole augmentation to reduce prolactin elevation or improve metabolic symptoms (Fleischhacker et al., 2010; Henderson et al., 2009; Shim et al., 2007)); management of behavioural disturbance (can be minimised with the use of single dose or 'stat' prescription rather than unlimited PRN use (Taylor et al., 2015)).

Changing the culture and ingrained habits of prescribing is difficult. In psychiatry poor prescribing has not been easy to address even when sustained and methodical efforts are made (Constantine et al., 2010a; Paton et al., 2008; Thompson et al., 2008). Change is possible, as other organisations have shown, through the use of sustained multidisciplinary quality improvement programmes (Mace & Taylor, 2015).

Thus far the studies in Chapters 2 and 3 have investigated the prescribing of antipsychotics in black and white patients only. In this analysis patients from *all* ethnicities (white, black, Asian, mixed, Chinese/other groups) were included to

determine if ethnicity, and other factors, predicted any of the prescribing outcomes. Although these groups make up a smaller proportion of the UK inpatient mental health population, differences in care has been reported (Care Quality Commission, 2010) making analysis of prescribing of antipsychotics for these populations necessary. Prescribing outcomes included dose, high dose and polypharmacy (both prescribed and administered to differentiate between regular and PRN use) as discussed above but also type of antipsychotic, clozapine use, route of administration and cost. This analysis allowed use of all of the data to determine if ethnicity, not just black and white, was a factor in prescribing of antipsychotics. It also allowed identification of whether certain patient factors associated with poorer prescribing could be targeted for improvements.

4.2 METHOD

This study was conducted in six mental health trusts in London, one in Nottingham and one in Manchester and analyses data from previous research. The details of the method are described extensively in Chapter 2.

In summary, data were collected for all adult inpatients on acute psychiatric wards in the eight UK trusts taking part in the study. Subjects were of all ethnicities i.e. black, white, Asian, mixed or other (as categorised by the most recent Office for National Statistics Census 2001 at the time of data collection) and were prescribed and taking one or more regular antipsychotics. Outcomes in the original study were total dose, high dose (more than 100% of BNF percentage maximum dose), type of antipsychotic (1^{st} or 2^{nd} generation), polypharmacy (both prescribed and administered) and cost. This analysis examines predictors of all these outcomes listed and, as well as these, included route of administration and clozapine use. These additional outcomes were included because reviewers of the previous study suggested them for inclusion as they have

previously been reported to be influenced by ethnicity (Kuno & Rothbard, 2002; Lloyd & Moodley, 1992; Whiskey et al., 2011). Data for these additional outcomes had already been collected and so could be extracted from the original dataset.

Medical and pharmacy staff at each trust performed the data collection and numerous confounding factors were gathered from case notes: age, legal status, substance misuse, diagnosis, duration of illness, education, employment status, forensic history, gender, compliance history, language, length of current admission, number of previous admissions, patient ethnicity, previous antipsychotic treatments, previous treatment with current antipsychotic, smoking status, weight. Other factors were collected from prescription charts including anticholinergic prescription, clozapine use, dose, length of treatment with current antipsychotic, polypharmacy prescribed, polypharmacy administered, type of antipsychotic, route of administration. How these confounders were defined for data collectors is described in Appendix 10.

4.2.1 Summary of Statistical Analysis

Multivariate linear regression was completed for dose and cost to determine the relationship between the variables collected (as described above) and continuous outcomes. Dummy variables were created for non-binary categorical classifications (only patient ethnicity had 3 categories – white, black, other (Asian, mixed, Chinese, other)) so they could be included in the multiple regression of continuous and categorical variables. For the remaining six categorical outcomes i.e. clozapine use (or not); high dose (or not); polypharmacy prescribed (or not); polypharmacy administered (or not); type of antipsychotic (FGA or SGA); route of administration (IM or oral) multivariate binary logistic regression was used. All outcome variables were binary and

the reference (or indicator) category was as follows; not clozapine, no high dose, no polypharmacy prescribed, no polypharmacy administered, FGA, IM route. Coding is as listed in the regression models.

The number of variables that can be included in a regression model depend on the amount of data collected. If too many variables are included then the model produced is unreliable. It is worth noting that variable numbers per cases of data rules simplify the issue as it is the magnitude of effect and the power required to detect this effect that are important. Nonetheless there are minimum cases per variable methods available. These include the often quoted 10-15 cases per predictor in a regression model (Field, 2013). Other experts (Green, 1991) recommend using overall fit (50 + (8 x predictor number)) and contribution of predictors (104 + predictor number). All three methods of calculation of sample size for number of variables were used and the largest case number chosen.

A 'power' calculation was performed before starting the study to determine sample size and avoid a false negative/type II error. A sample size of 788 was calculated to be required to have an 80% chance of detecting a 5 percentage point (55% vs. 50%) difference for the main outcome (percentage maximum dose) between black and white patients (assuming a standard deviation of 25). Sample size was not calculated for the outcome of cost.

Previous research studies measuring associations between antipsychotic prescribing and ethnicity were examined and tabulated to determine which variables were important to include in the model i.e. which variables predicted or adjusted outcomes (see Appendix

2). Then each variable was entered into a simple univariate regression model to determine the strength of the relationship between predictor and outcome. All variables with a significance of $p<0.05$ were then included in a multivariate regression model using a backward method (likelihood ratio (LR) for logistic method, entry $p<0.05$, removal $p<01$) with a complete cases dataset. Variables derived from the outcomes were not included in the model to avoid high correlation and non-independence. Where patient ethnicity was not significantly associated with outcome it was still included in the model as it was the predictor of interest in the study. Finally significant variables from this method were included in each model using the enter method. Non-significant variables were removed singly in order of least significance until a final parsimonious model was determined.

Data were checked for outliers using descriptive statistics, casewise diagnostics and graphical boxplot representation. Outliers were also checked for accuracy and included if clinically important. Two-way interactions between variables included in the model were tested for association. Interactions of significance were then added to the final model using the forced entry method with the higher order variables. Each interaction was examined for statistical significance at the 5% level.

Linear regression assumptions were tested graphically for linear relationships between continuous variables and outcomes, normally distributed errors and homoscedasticity (i.e. residuals having similar variance). Then multicollinearity (i.e. no perfect linear relationship between variables) was checked for by examining correlations between variables and collinearity diagnostics i.e. VIF, tolerance and eigenvalues. The outcome values came from separate entities so were independent but high dose and cost were not included as variables in the dose model as not independent. Likewise high dose and

total dose were not included in the cost model for the same reason. Finally independence of errors (i.e. residuals should be uncorrelated) was tested using the Durbin-Watson test for serial correlations between errors.

Logistic regression assumptions were tested as follows:

Linearity of logit (i.e. each variable must be linearly related to the natural log of outcomes). This was tested by calculation of the quartiles for continuous predictors to make a categorical variable, then fitting a logistic regression model replacing the continuous variable with the 4-point categorical one, plotting estimated coefficients vs. midpoints of the groups and connecting the points. Finally the plot was visually inspected to check if linear and passed assumption. If not linear then the variable was transformed. (Hosmer & Lemeshow, 2000).

Multicollinearity (i.e. predictors should not be too highly correlated) was checked with tolerance, VIF, eigenvalues, condition indices and variance proportions. IBM SPSS does not produce collinearity diagnostics for logistic regression so these were obtained by running a linear regression of categorical outcomes and the same predictors used in the logistic regression above. The condition index is the square root of the ratio of the largest eigenvalue to the eigenvalue of interest. There is no limit as to how large a condition index needs to be to indicate a problem but they should be broadly similar. Variance proportions are the proportion of the variance of each predictors regression coefficient attributed to each eigenvalue. Predictors that have high proportions on the same small eigenvalue (conversely the highest eigenvalue number) indicate that the variances of their regression coefficients are dependent.

Independence of errors (i.e. cases of data should not be related). Violating this assumption causes overdispersion (the observed variance is larger than expected from the logistic regression model). This results in limited standard errors and narrower confidence intervals for the test statistics of predictors in the model and increases the risk of type I (false positive) errors.

Model fit (i.e. how well model fits the data and predicts outcome) for linear regression was evaluated with R^2 (i.e. multiple correlation coefficient squared) and for logistic regression was assessed by calculating several measures. These were the omnibus test of model coefficients i.e. the difference between the -2 log-likelihood values of the basic constant only model and the model with predictors included. Also Cox and Snell's R^2 and Nagelkerkes R^2 which give an indication of the measure of explained variation of the model. Both were calculated as Nagelkerke's is a more reliable measure than Cox and Snell's. Then the Hosmer and Lemeshow test comparing observed and expected events in each group using chi-squared was completed. Finally a classification table and plot (histogram of the predicted probabilities) were produced for each model.

Residuals were examined so that cases that fit the model poorly and those exerting undue influence could be identified. Poorly fitting cases were identified using Studentized (unstandardised residual divided by an estimate of its standard deviation) and standardised residuals. Studentized residuals are more precise than standardized residuals and the number of cases more than 2.5 should number less than 1% to ensure good representation of the data. For standardised residuals (residuals expressed in standard deviation units), cases more than 2 should number less than 5% for the same reason. Those cases exerting undue influence in the model were then examined using

Cook's distance statistic (i.e. measure of influence of a case on the model, should be less than 1); leverage statistics (i.e. influence of observed value of outcome over predicted value, range from 0 to 1, calculated as no of predictors in model + 1/divided by sample size) - three times the average leverage value is a suggested cut-off for examining cases with excess influence; absolute DFBeta (measures the influence of a case on the coefficients of the regression model), should be less than 1.

Several sensitivity analyses were conducted for all models. These were for missing data, variables chosen for inclusion in model, outlier inclusion and exclusion and interaction inclusion and exclusion.

4.3 RESULTS

4.3.1 STUDY POPULATION

Demographic and patient variable details for the total sample are described in Tables 34 and 35. Data were collected for a total of 1198 patients. Overall 332 (27.2%) patients had at least one unrecorded demographic detail. There were 866 (72.3%) complete cases used in this analysis.

Sample sizes were calculated as follows (including dummy variables), for dose between 123 to 285, for cost 119 and 225, for clozapine use116 to 180, for high dose 116 to 180, for polypharmacy prescribed 120 to 240, for polypharmacy administered 118 and 210, for type of antipsychotic 120 to 240 and for route of administration 120 to 240. The complete case sample was 978 for dose, 1032 for cost, 1023 for clozapine use, 909 high dose, 1071 polypharmacy prescribed, 1081 polypharmacy administered, 996 type of antipsychotic, 1070 route of administration and so the data set was larger than the minimum number of cases needed and enough to include all covariates.

Most patients were from non-SLaM centres, male, of non-white ethnicity, had English as a first language, had completed secondary school education, were not employed, smokers, not misusing substances, were diagnosed with schizophrenia, had no forensic history, a white consultant psychiatrist, were detained in hospital, with two or more previous admissions and a history of medication non-compliance. They were taking oral, SGA monotherapy (but not clozapine), no anticholinergic medication, had taken their current antipsychotic before and had taken two or more antipsychotics previously.

TABLE 34 DEMOGRAPHIC AND CLINICAL DETAILS

Variable		n (%)	Missing (%)
Centre	SLaM	228 (19)	0 (0)
	Not SLaM	970 (81)	
Gender	Female	427 (35.6)	0 (0)
	Male	771(64.4)	
Patient ethnicity	White	562 (46.9)	17 (1.4)
	Black	410 (34.2)	
	Other (Asian, mixed, Chinese/other)	209 (17.4)	
Employment	Not employed	1127 (94.1)	22 (1.8)
	Employed	49 (4.1)	
Education	Secondary	618 (51.6)	105 (8.8)
	Other	475 (39.6)	
Language	Not English	168 (14)	34 (2.8)
	English	996 (83.1)	
Smoking status	Non-smoker	325 (27.1)	55 (4.6)
	Smoker	818 (68.3)	
Diagnosis	Not schizophrenia	329 (27.5)	76 (6.3)
	Schizophrenia	793 (66.2)	
Ethnicity of consultant	White	768 (64.1)	45 (3.8)
	Not white	385 (32.1)	
Previous treatment with current antipsychotic	No	382 (31.9)	138 (11.5)
	Yes	678 (56.6)	
Legal status	Sectioned	824 (68.8)	6 (0.5)
	Informal	368 (30.7)	
Forensic history	No	636 (53.1)	87 (7.3)
	Yes	475 (39.6)	
Previous number of antipsychotic treatments	0 or 1	468 (39.1)	178 (14.9)
	2 or more	552 (46.1)	
Previous admissions	0 or 1	254 (21.2)	83 (6.9)
	2 or more	861 (71.9)	
History of medication non-compliance	No	227 (18.9)	77 (6.4)
	Yes	894 (74.6)	
Route of administration	Intramuscular	280 (23.4)	0 (0)
	Oral	918 (76.6)	
Clozapine use	No	1074 (89.6)	0 (0)
	Yes	124 (10.4)	
Type of antipsychotic	FGA	284 (23.7)	0 (0)
	SGA	914 (76.3)	
Polypharmacy prescribed	No	640 (53.4)	1 (0.1)
	Yes	557 (46.5)	
Polypharmacy administered	No	911 (76)	29 (2.4)
	Yes	258 (21.5)	

Variable		n (%)	Missing (%)
Anticholinergic use	No	963 (80.4)	41 (3.4)
	Yes	194 (16.2)	
Substance Misuse	No	628 (52.4)	57 (4.8)
	Yes	513 (42.8)	

TABLE 35 CONTINUOUS DEMOGRAPHIC AND CLINICAL VARIABLES

Variable	Median	Missing (%)
Age (years; range)	38 (18-76)	2 (0.2)
Weight (kg; range)	77.8 (33-175.7)	156 (13)
Length of hospital admission (days; range)	56 (1-4210)	31 (2.6)
Duration of illness (days; range)	3285 (1-18250)	131 (10.9)
Duration of current antipsychotic therapy (days; range)	30 (1-7300)	146 (12.2)
Total antipsychotic dose (% maximum; range)	55.5 (2.5-272.5)	41 (3.4)
Cost of antipsychotic treatment (£ for 28 days; range)	87.82 (1.40-632.26)	40 (3.3)

4.3.2 Total Dose and Cost Outcomes

The analysis used complete cases and the process of choice of variables for each model is described in the section 4.2.1. Missing data case numbers for variables included in the development of the models represented more than 5% of the study population (for dose - complete cases 978/1198 total data cases, 81.6% of the total data; for cost - complete cases 1032 /1198 total data, 86.1% of total sample). No effect of missing data on total dose or cost was found in a sensitivity analysis.

4.3.2.1 Variable choice

The variables significantly associated ($p<0.05$) with log total dose and log cost are listed in Table 36. Categorical variable categories were collapsed to enable model fit. Patient ethnicity was not significantly associated with dose or cost but was included in the model as it is the outcome of interest. The outcome values came from separate entities so were independent but high dose and cost were not included as variables in the dose

model as not independent. Likewise high dose and total dose were not included in the cost model for the same reason.

TABLE 36 VARIABLES ASSOCIATED WITH LOG TOTAL DOSE AND LOG COST OUTCOMES

Outcome	**Variable**		**p**
Log total dose	Gender		0.001
	Smoking status		0.01
	Diagnosis		<0.001
	Legal status		0.001
	Forensic history		0.03
	Number of previous antipsychotics		0.019
	Number of previous admissions		<0.001
	Compliance history		<0.001
	Route of administration		0.001
	Anticholinergic use		<0.001
	Substance misuse		0.006
	Type of antipsychotic		<0.001
	Clozapine use		0.001
	Polypharmacy prescribed		<0.001
	Duration of illness (log)		0.013
	Weight (log)		<0.001
	Length of admission (log)		<0.001
	Patient ethnicity (including dummy variables for black and other ethnicity)	Black	0.402
		Other	0.164
Log cost	Diagnosis		0.001
	Ethnicity of consultant		0.018
	Legal status		0.035
	Previous number of antipsychotics		0.034
	Previous number of admissions		<0.001
	Compliance history		<0.001
	Route of administration		0.011
	Anticholinergic use		0.001
	Type of antipsychotic		<0.001
	Clozapine use		<0.001
	Polypharmacy prescribed		<0.001
	Weight (log)		<0.001
	Length of admission (log)		0.003
	Patient ethnicity (including dummy variables for black and other ethnicity)	Black	0.856
		Other	0.138

4.3.2.2 OUTLIERS

Casewise diagnostics for log total dose outcome found fewer than 5% of cases had standardised residuals of 2 or more (43/978 in model), fewer than 1% of cases had standardised residual of 3 or more in the model (8/978 in model), no Cook's distance statistic was more than 1 and 99.8% of cases were fewer than the average leverage value. For log cost outcome fewer than 5% of cases had standardised residuals of 2 or more (46/1032 in model), fewer than 1% of cases with standardised residual of 3 or more (7/1032 in model), no Cook's distance statistic more than 1 and 98.8% of cases fewer than the average leverage value. Outliers were included in the dose and cost models as both models predictive capacity was only marginally improved when removed.

4.3.2.3 INTERACTION EFFECTS

Inclusion of interactions removed higher order variables from the model and had little impact on predictive power so were not included.

4.3.2.4 LINEAR REGRESSION ASSUMPTIONS

i. A linear relationship between variables and dose and cost outcomes was made possible by a log transformation of some continuous predictors i.e. weight, length of admission, duration of illness.

ii. Errors (i.e. residuals) were normally distributed and tested graphically with a P-P plot and histogram for log total dose and log cost. P-P (observed probability vs. expected probability) plots produced a relatively straight line. Histograms were normally distributed.

iii. Log transformation of total dose and cost outcomes ensured residuals were homoscedastic. Scatterplot graphs of ZRESID (standardised residuals) against

ZPRED (standardised predicted values of outcome based on the model) showed a random array evenly dispersed around zero - they were not funnelled or curved.

iv. No multicollinearity. Pearson correlation, highest value 0.332 for dose and 0.633 for cost, none more than +/- 0.9. The VIF highest value 1.192 for dose and 1.410 for cost, none more than 10. Tolerance (1/VIF) lowest value is 0.839 for dose and 0.709 for cost, neither less than 0.2. Predictors have variance loading on different eigenvalue dimensions.

v. Errors were independent and uncorrelated as the Durbin-Watson test for dose model was 1.901 and cost 1.964 (not less than 1 or more than 3).

4.3.2.5 CAUSES OF ASSOCIATIONS WITH LOG TOTAL DOSE

Associations with higher log total dose (see Table 37) were; larger weight, greater number of previous admissions, longer length of admission, non-compliance with medication and use of a SGA. Taking clozapine was associated with a lower log total dose than not taking clozapine.

4.3.2.6 CAUSES OF ASSOCIATIONS WITH LOG COST

Associations with higher log cost (see Table 38) were; greater number of previous admissions, longer length of admission, non-compliance with medication, intramuscular route of administration, use of a SGA and greater use of prescribed polypharmacy.

4.3.2.7 LOG TOTAL DOSE AND LOG COST MODELS

TABLE 37 LINEAR REGRESSION MODEL LOG TOTAL DOSE OUTCOME (ALL ETHNICITIES)

Variables	Coefficient B	Standard Error	p-value	95% Confidence Interval for B	
				Lower Bound	Upper Bound
Constant	0.95	0.41	0.021	0.15	1.76
Weight (log)	0.45	0.09	0.001	0.26	0.63
Previous admissions; 2 or more	0.30	0.06	0.001	0.19	0.42
Length of admission (log)	0.10	0.02	0.001	0.06	0.13
Compliance history; non-compliant	0.19	0.06	0.001	0.08	0.30
Clozapine use; yes	-0.35	0.08	0.001	-0.50	-0.20
Type of antipsychotic; 2nd generation	0.44	0.05	0.001	0.34	0.55

n=978, R^2 0.153

The model explains only 15.3% (R^2 0.153) of variation in the data. Dependent variable is total dose (log).

TABLE 38 LINEAR REGRESSION MODEL LOG COST OUTCOME (ALL ETHNICITIES)

Variables	Coefficient B	Standard Error	p-value	95% Confidence Interval for B	
				Lower Bound	Upper Bound
Constant	2.41	0.11	0.001	2.20	2.62
Previous admissions; 2 or more	0.26	0.06	0.001	0.15	0.37
Length of admission (log)	0.09	0.02	0.001	0.06	0.13
Compliance history; non-compliant	0.17	0.06	0.005	0.05	0.28
Route; oral	-0.67	0.06	0.001	-0.80	-0.55
Type of antipsychotic; 2nd generation	2	0.06	0.001	1.88	2.12
Polypharmacy prescribed; yes	0.39	0.05	0.001	0.33	0.48

n=1032, R^2 0.553

Model can predict 55.3% ($R^2 = 0.553$) of the variability of cost. Dependent variable is cost (log).

4.3.3 CLOZAPINE USE, HIGH DOSE, POLYPHARMACY PRESCRIBED, POLYPHARMACY ADMINISTERED, TYPE OF ANTIPSYCHOTIC AND ROUTE OF ADMINISTRATION OUTCOMES

The analysis used complete cases and the process of choice of variables for each model is described in section 4.2.1. Missing data case numbers (for variables included in model) are more than 5% of the study population (for clozapine use complete cases 1023 /1198 total data cases; 909/1098 for high dose; 1071/1198 for polypharmacy prescribed; 1081/1198 for polypharmacy administered; 996 /1198 for type of antipsychotic and 1070/1198 for route of administration). No significant effect of missing data on clozapine use, high dose, polypharmacy prescribed, polypharmacy administered, type of antipsychotic or route of administration was found in this analysis.

4.3.3.1 VARIABLE CHOICE

The predictors significantly ($p<0.05$) associated with each outcome are listed in Table 39. Variables not included in model for clozapine use were type and route of antipsychotic; for high dose - total dose, cost, weight and length of admission (the latter two removed as violated assumption of linearity of logit); for polypharmacy prescribed – polypharmacy administered, cost and high dose; for polypharmacy administered - polypharmacy prescribed, cost and high dose; for type of antipsychotic - polypharmacy prescribed, clozapine use, cost and high dose; for route of administration - polypharmacy prescribed, clozapine use and cost.

For the outcome of clozapine use, three preliminary models were constructed. The first included all significant variables and initially the model fitted the data but after outliers were removed this was not the case. Removal of employment status from this first model because of large standard errors also did not allow a model to be fitted to the

data. In the second model centre, employment status, diagnosis and number of previous antipsychotics predictors were removed again because of large standard errors. A model was initially fitted but when outliers removed could not be fitted to the data. In a third model variables were removed as in models 1 and 2 but now also patient ethnicity and number of previous admissions because of large standard errors. This model fitted the data both with and without outliers but was a poor quality model with no significant predictors.

For high dose outcome the following attempts were made to fit a model. Model one included significant predictors listed in Table 39 but when outliers removed would not fit to the data. A second model used variables that, in expert opinion, would be expected to predict the outcome. Again outliers were fitting the model to the data.

TABLE 39 VARIABLES ASSOCIATED WITH CLOZAPINE USE, HIGH DOSE, POLYPHARMACY PRESCRIBED, POLYPHARMACY ADMINISTERED, TYPE OF ANTIPSYCHOTIC AND ROUTE OF ANTIPSYCHOTIC OUTCOMES

Outcome	Variable	p
Clozapine use	Centre	0.038
	Employment status	0.016
	Diagnosis	<0.001
	Number of previous antipsychotics	<0.001
	Number of previous admissions	0.003
	Duration of illness	0.01
	Weight	0.014
	Length of admission	0.001
	Length of treatment	0.017
	Patient ethnicity	0.287
High dose	Diagnosis	0.003
	Previous treatment with current antipsychotic	<0.001
	Forensic history	0.005
	Number of previous antipsychotics	0.002
	Number of previous admissions	0.001
	Compliance status	0.001
	Polypharmacy prescribed	<0.001
	Polypharmacy administered	<0.001
	Patient ethnicity	0.766
Polypharmacy prescribed	Centre	<0.001
	Gender	0.006
	Smoking status	0.002
	Diagnosis	0.005
	Legal status	<0.001
	Forensic history	<0.001
	Number of previous admissions	0.019
	Compliance history	0.002
	Route of administration	0.001
	Anticholinergic use	0.003
	Substance misuse	<0.001
	Total dose	<0.001
	Age	0.012
	Weight	<0.001
	Patient ethnicity	0.042

Outcome	Variable	p
Polypharmacy Administered	Centre	0.005
	Diagnosis	0.001
	Legal status	0.005
	Forensic history	0.004
	Number of previous antipsychotics	0.014
	Number of previous admissions	<0.001
	Compliance history	<0.001
	Route of administration	<0.001
	Anticholinergic use	<0.001
	Total dose	<0.001
	Type of antipsychotic	0.008
	Weight	<0.001
	Patient ethnicity	0.234
Type of antipsychotic	Smoking status	0.033
	Diagnosis	0.01
	Ethnicity of consultant	0.039
	Legal status	0.01
	Forensic history	<0.001
	Number of previous antipsychotics	<0.001
	Number of previous admissions	<0.001
	Compliance history	<0.001
	Route of administration	<0.001
	Anticholinergic use	<0.001
	Total dose	<0.001
	Polypharmacy administered	0.008
	Weight	0.019
	Duration of illness	<0.001
	Patient ethnicity	0.033
Route of administration	Diagnosis	<0.001
	Legal status	<0.001
	Forensic history	<0.001
	Number of previous antipsychotics	0.001
	Number of previous admissions	<0.001
	Compliance history	<0.001
	Anticholinergic use	<0.001
	Total dose	0.012
	Polypharmacy administered	<0.001
	Age	0.029
	Duration of illness	<0.001
	Weight	0.013
	Length of admission	<0.001
	Patient ethnicity	0.001

4.3.3.2 ASSESSMENT OF MODEL FIT

The full results of assessment of model fit are in Table 40. The omnibus tests of model coefficients (i.e. the log-likelihood) of models with predictors were very large (indicating poorly fitting statistical models) for all outcomes and were mostly only slightly, but statistically significantly ($p<0.001$ for each model) better than with the constant alone.

The Hosmer and Lemeshow test results were statistically insignificant for most of the outcomes meaning there were no significant difference between observed and expected values and the models fit data reasonably well. The exception was for polypharmacy administered outcome which did not fit data well.

Classification table results show that the models for most outcomes were slightly better at predicting the results than when the constant only was included.

The classification histogram plots of predicted probabilities were incorrect for polypharmacy prescribed outcome. This is because for polypharmacy prescribed many of the cases with a predicted probability of 'yes prescribed polypharmacy' were clustered in the 'no' part of the histogram and vice versa. Results were better for the other outcomes; polypharmacy administered' were broadly correct as the predicted probability for 'no polypharmacy administered' outcome was clustered in the 'no' part of the histogram however some of the 'yes polypharmacy administered' were in the 'no' probability portion of the graph; type of antipsychotic was broadly correct as the predicted probabilities for both outcomes are clustered at each end of the histogram in the correct places; route was broadly correct as the predicted probability for oral route

outcome was clustered on the oral side of the histogram but IM route was spread on both the IM and oral sides so the model's prediction of IM route was less accurate.

TABLE 40 ASSESSMENT OF MODEL FIT

Outcome	Methods of assessment of model fit						
	Omnibus test of model coefficients -2 log-likelihood		Cox and Snell's R^2	Nagelkerke's R^2	Hosmer and Lemeshow test p value	Classification Table	
	Model with predictors	Constant only model				Model with predictors	Constant only model
Polypharmacy prescribed	1306.14	1476.69	0.147	0.197	0.349	66.5%	54.2%
Polypharmacy administered	833.63	1116.43	0.230	0.357	0.001	84.7%	78.8%
Type of antipsychotic	798.94	1135.29	0.287	0.421	0.083	82.7%	74.3%
Route of administration	862.53	1172.80	0.252	0.378	0.613	82.7%	76.3%

4.3.3.3 OUTLIERS

Outliers (more than 2 standardised residuals from regression line) for polypharmacy prescribed (n=1), polypharmacy administered (n=44), type of antipsychotic (n=38), route of administration (n=37) were excluded from the model, the analyses rerun and models refit. Exclusion produced a model that fit the data slightly better for polypharmacy prescribed, polypharmacy administered, type of antipsychotic and route of administration. The polypharmacy administered outlier free model had the same variables as the model with outliers included but also centre, route and anticholinergic use. Whilst for type of antipsychotic the outlier free model fit the data with the same significant predictors but also included number of previous admissions. Outliers were still included for all five models as they were part of the natural variation of the data and exclusion improved model accuracy only marginally.

4.3.3.4 INTERACTION EFFECTS

No interactions were significantly associated with polypharmacy prescribed, polypharmacy administered and route of administration so were not included in the final model. Two interactions were significantly associated with type of antipsychotic i.e. polypharmacy administered and anticholinergic use, total dose and anticholinergic use. When these interactions were included in the model they caused the removal of anticholinergic use (a higher order variable) so were not included in the final model.

4.3.3.5 LOGISTIC REGRESSION ASSUMPTIONS

i. Linearity of logit

There are two continuous variables in the models polypharmacy prescribed and route of administration (age and total dose); one continuous variable in the polypharmacy administered and type of antipsychotic models (total dose). Using

the Hosmer and Lemeshow method (Hosmer & Lemeshow, 2000), the graphs for total dose and age were linear.

ii. Multicollinearity

Pearson's correlation checked, none more than +/- 0.9;
variance inflation factor (VIF) values, none more than 10;
tolerance (1/VIF) values, none below 0.1 for all models.

Eigenvalues were similar overall for almost all for polypharmacy prescribed (except eigenvalue on dimension 1 of 5.231, other values less than 1), polypharmacy administered (except eigenvalue value 3.451 on dimension 1), type of antipsychotic (except eigenvalue 3.765 on dimension 1 and route of administration (except eigenvalue 5.387 on dimension 1)

Condition indices were broadly similar except for polypharmacy prescribed model on dimension 7 condition index is 16.629 other values were less than 9; route of administration model on dimension 7 of 12.379; polypharmacy administered and type of antipsychotic models were broadly similar.

The polypharmacy administered, type of antipsychotic and route of administration models variance proportions were evenly spread over the smallest eigenvalues. The polypharmacy prescribed models variance proportions were evenly spread over the smallest eigenvalues apart from centre which had a relatively high variance proportion 0.63 on dimension 6 and 7.

4.3.3.6 RESIDUAL ANALYSIS

Studentized residual, number of cases more than 2.5 for polypharmacy prescribed 1/1071, 0.1% of sample; polypharmacy administered 44/1081, 4.1%; type of antipsychotic 38/996, 3.8%; route of antipsychotic 37/1070, 3.5%.

Standardised residuals number of cases over 2 for polypharmacy prescribed 1/1071, 0.1% of cases; polypharmacy administered 83/1081, 7.7%; type of antipsychotic zero cases; route of administration 89/1070, 8.3%.

No Cook's distance statistic was more than 1 for polypharmacy prescribed, polypharmacy administered, type of antipsychotic or route of antipsychotic models. Leverage values were, for polypharmacy prescribed model 99.6%; polypharmacy administered 91.5%; type of antipsychotic 99.3%; route of administration 99.4%.

Absolute DFBeta were less than 1 for all cases for polypharmacy prescribed, polypharmacy administered, type of antipsychotic, route of administration.

4.3.3.7 CAUSES OF ASSOCIATIONS WITH CLOZAPINE USE

No significant predictors of taking clozapine were identified from analysis of this dataset.

4.3.3.8 CAUSES OF ASSOCIATIONS WITH HIGH DOSE

No significant predictors of high dose were identified from analysis of this dataset. It was not possible to fit a model to the data for high dose outcome.

4.3.3.9 CAUSES OF ASSOCIATIONS WITH POLYPHARMACY PRESCRIBED

Associations with being prescribed more than one antipsychotic (see Table 41) were; non-South London and Maudsley NHS trust centre (SLaM), the subject having a forensic history and a higher total dose. Younger age, not being detained under a Mental Health Act section and oral route were predictors of prescribed antipsychotic monotherapy.

4.3.3.10 CAUSES OF ASSOCIATIONS WITH POLYPHARMACY ADMINISTERED

Associations with being administered more than one antipsychotic (see Table 42) were; greater number of previous admissions and a higher total dose. SGA use predicted being administered monotherapy.

4.3.3.11 CAUSES OF ASSOCIATIONS WITH TYPE OF ANTIPSYCHOTIC

Associations with SGA use (see Table 43) were; oral route, higher total dose, being administered only one antipsychotic, having had fewer previous antipsychotics and no anticholinergic use.

4.3.3.12 CAUSES OF ASSOCIATIONS WITH ROUTE OF ADMINISTRATION

Associations with oral route (see Table 44) were; not being sectioned under the Mental Health Act, SGA use, younger age, non-schizophrenia diagnosis, fewer previous admissions and a lower total dose.

4.3.3.13 POLYPHARMACY PRESCRIBED, POLYPHARMACY ADMINISTERED, TYPE OF ANTIPSYCHOTIC AND ROUTE OF ADMINISTRATION MODELS

TABLE 41 LOGISTIC REGRESSION MODEL POLYPHARMACY PRESCRIBED (ALL ETHNICITIES)

Variables	B	Standard Error	p-value	Odds Ratio	95% CI for Odds Ratio	
					Lower	Upper
Constant	-0.87	0.33	0.008	0.42	N/A	N/A
Centre; non-SLaM	0.80	0.17	0.001	2.23	1.60	3.11
Age	-0.02	0.01	0.001	0.98	0.97	0.99
Forensic history; yes	0.34	0.14	0.015	1.40	1.07	1.84
Section status; not sectioned	-0.42	0.15	0.005	0.66	0.49	0.88
Route of administration; oral	-0.40	0.16	0.012	0.67	0.49	0.92
Total dose	0.02	0.002	0.001	1.02	1.01	1.02

n= 1071, -2 log-likelihood = 1306.144 ,CI = confidence intervals, N/A = not applicable.

TABLE 42 LOGISTIC REGRESSION MODEL POLYPHARMACY ADMINISTERED (ALL ETHNICITIES)

Variable	B	Standard Error	p-value	Odds Ratio	95% CI of Odds Ratio	
					Lower	Upper
Constant	-3.68	0.32	0.001	0.03	N/A	N/A
Previous admissions; 2 or more	0.59	0.26	0.02	1.78	1.09	2.98
Type of antipsychotic; 2nd generation	-1.07	0.20	0.001	0.34	0.23	0.51
Total dose	0.04	0.01	0.001	1.03	1.03	1.04

n = 1081, -2 log-likelihood = 833.632, CI = confidence interval. N/A = not applicable.

TABLE 43 LOGISTIC REGRESSION MODEL TYPE OF ANTIPSYCHOTIC (SGA, ALL ETHNICITIES)

Variables	B	Standard Error	p-value	Odds Ratio	95% CI for Odds Ratio	
					Lower	Upper
Constant	-1.27	0.26	0.001	0.28	N/A	N/A
Route; oral	2.64	0.20	0.001	14.08	9.51	20.83
Polypharmacy administered; yes	-0.89	0.24	0.001	0.41	0.26	0.66
Previous number of antipsychotics; 2 or more	-0.55	0.18	0.003	0.58	0.40	0.83
Anticholinergic use; yes	-1.42	0.23	0.001	0.24	0.16	0.38
Total dose	0.02	0.003	0.001	1.02	1.02	1.03

n= 996, -2 log-likelihood = 798.936, CI = confidence interval, N/A = not applicable

TABLE 44 LOGISTIC REGRESSION MODEL ORAL ROUTE OF ADMINISTRATION (ALL ETHNICITIES)

Variables	B	Standard Error	p-value	Odds Ratio	95% CI for Odds Ratio	
					Lower	Upper
Constant	1.80	0.41	0.001	6.06	N/A	N/A
Age	-0.02	0.01	0.022	0.98	0.97	0.99
Diagnosis; schizophrenia	-0.99	0.22	0.001	0.37	0.24	0.57
Section status; not sectioned	0.64	0.21	0.002	1.90	1.26	2.86
Previous admissions; 2 or more	-0.75	0.26	0.004	0.47	0.28	0.79
Type of antipsychotic; 2nd generation	2.57	0.19	0.001	13.09	9.08	18.86
Total dose	-0.007	0.002	0.001	0.99	0.98	0.99

n= 1070, -2 log-likelihood = 862.526, CI = confidence interval, N/A = not applicable

4.4 DISCUSSION

4.4.1 MAIN FINDINGS

The most important finding was that ethnicity was not associated with any of the study's multiple outcomes but the significant limitations of the study may have resulted in negative findings. The number of outcomes was extended from previous analyses and included clozapine use and route of administration thus providing a more comprehensive assessment of the effect of ethnicity on prescribing of antipsychotics.

Given that ethnicity was not associated with any of the outcomes, it is worth examining the other factors that did affect antipsychotic prescribing. Dose equivalence of antipsychotics can be expressed in many ways. The most commonly used methods are chlorpromazine equivalents, defined daily dose and percentage maximum dose. Historically the CPZe method is used. Chlorpromazine is a low potency, FGA with a large dose range (25 to 1000mg) (British Medical Journal Group and Pharmaceutical Press, 2014). Doses of other FGAs were converted to chlorpromazine doses to allow comparison. The conversion ratios were based on dopamine receptor occupancy rates *in vitro*, often had hugely different quoted equivalences and relied for legitimacy through repetition in the published literature (Yorston & Pinney, 2000). High doses are described as being more than 1g CPZe (British Medical Journal Group and Pharmaceutical Press, 2014) but some authors suggest they may be as low as 600mg CPZe (Buchanan et al., 2010). DDD is the average daily maintenance dose per day of a medication when used for its main indication in adults. It is calculated by dividing the prescribed daily dose by the defined daily dose. DDD is defined by the WHO and is based on systematic review of the literature but does not take into account differences in starting doses of antipsychotics, is costly to access and can result in erratic

recommendations (Gardner et al., 2010). The percentage maximum dose method calculates each dose as a proportion of the BNF maximum dose. It is a useful practical measure as it is directly related to the legalities of prescribing and clinical practice. Comparison of these methods has yielded inconsistent results. Some authors report discrepancies between methods (Patel et al., 2013; Rijcken et al., 2003) whilst others describe coherence (Nose et al., 2008). It is unsurprising that, given these differences, expert consensus opinions are also sometimes used (Gardner et al., 2010). Choice of an antipsychotic dose equivalence method requires justification depending on the study being undertaken (see Chapter 2).

Higher total doses were prescribed to patients of larger weight, those not compliant with medication, on SGAs, with a longer length of admission and a greater number of previous admissions. Let us look at each of these in turn. The metabolic effects of antipsychotics, particularly those from the 2nd generation (Rummel-Kluge et al., 2010), are well known and may account for why larger weight was associated with higher total doses. In addition larger patients may affect prescriber's perception of the magnitude of dose needed and so also be associated with higher doses. Non-compliance is often undetected by prescribers and may result in them increasing doses of antipsychotics through perceived lack of effect of a treatment. Moreover not taking antipsychotic treatment greatly increases the risk of relapse which often leads to the prescribing of relatively higher acute doses (Harrington et al., 2002; Wyatt, 1991).

The association of SGA use with higher doses was surprising. This is because doses of newer antipsychotics are well studied and clearly described, making it more difficult for prescribers to inadvertently prescribe larger doses. The estimates of minimum effective

doses and dose ranges of older FGAs have reduced over recent years. This is because neuroimaging studies have shown that much lower levels of dopamine blockade are needed for efficacy of antipsychotics than was previous recognised (Kapur et al., 2000). Haloperidol provides a good example when compared with olanzapine. The maximum dose of haloperidol at the time of data collection was 30mg/day (now 20mg/day and previously 200mg/day (British Medical Association and Royal Pharmaceutical Society of Great Britain, 2008)) whilst the effective dose of olanzapine is probably 10-15mg (Davis & Chen, 2004) and maximum is 20mg. Thus proportionally an effective dose of haloperidol of 5mg was 16% of the maximum dose at the time of the data collection whilst olanzapine was 50-75%.

Chronicity of illness is represented by predictors of a longer length of admission and a greater number of previous admissions - factors that describe relapse and thus increased doses (Leucht et al., 2013). Finally clozapine use predicted a lower total dose possibly because of a lower risk of polypharmacy and better efficacy (Kane et al., 1988) and risks associated with combinations with clozapine. Unfortunately it was not possible to fit the data into a good quality model for clozapine use to test this theory and clozapine use was not a predictor of polypharmacy prescribed or polypharmacy administered outcomes.

Higher costs of antipsychotic treatment were associated with a greater number of previous admissions (as doses are increased when people are admitted (Taylor et al., 2015)), a longer length of admission, prescribed polypharmacy and a history of non-compliance – all factors indicating a more severe and enduring illness, higher doses and thus greater costs. The oral route of administration was associated with lower costs

probably owing to higher costs of depot treatments. SGA are more expensive than FGA so it was unsurprising that SGA were associated with higher costs.

Antipsychotic polypharmacy was associated with higher total doses, greater number of previous admissions, having a forensic history and non-SLaM centre. Antipsychotic monotherapy was predicted by younger age, not being detained under a Mental Health Act section, oral route of administration and use of a SGA. As discussed in the introduction to this chapter antipsychotic polypharmacy often results in higher doses (Harrington et al., 2002) and unfortunately both are commonly prescribed in the UK (Paton et al., 2008). As with higher doses a greater number of previous admissions was associated with polypharmacy, given multiple admissions are likely to indicate a more severe and chronic illness. Those patients with a forensic history may be more at risk of antipsychotic combinations, high dose use and use of multiple routes (Barnes et al., 2009; Lelliott, 2002). This is possibly because of lack of efficacy of a single agent (especially if this is a depot) and prescribers concern about patients' risk histories (Grech & Taylor, 2012; Stubbs et al., 2006). The effects of centre on polypharmacy were interesting as non-SLaM NHS trusts were more likely to prescribe in this way. A previous study had also found a non-SLaM centre effect of polypharmacy – a result of particularly high polypharmacy rates in one centre (Connolly & Taylor, 2008). It is worth noting that centre only had an effect on polypharmacy prescribed not polypharmacy administered. The effect of non-SLaM centre may have been because of concerted efforts to improve polypharmacy prescribing in SLaM through a quality improvement programme. This paid particular attention to eliminating routine prescription of PRN antipsychotics for behavioural management (Mace & Taylor, 2015).

Not being detained and being of younger age were associated with antipsychotic monotherapy. Both of these predictors, as with length of admission and number of previous admissions, suggest a less severe illness presentation and so a lower likelihood of antipsychotic polypharmacy use. Prescribers often use antipsychotic polypharmacy when faced with a severely unwell patient who is not responding to a single agent. They are under pressure to find an effective treatment and polypharmacy can be an inadvertent consequence rather than a rational evidence-based decision. Interestingly this result differs from the black and white data analysis in Chapter 2 where a younger age was associated with increased risk of antipsychotic polypharmacy. The addition of another ethnic group, of relatively small numbers compared with the black and white groups, is a factor in the conflicting results. There have been concerns that young, black patients are perceived stereotypically as more violent than other ethnic groups possibly accounting for the differing results (Prins 1993). Unusually SGA use was also associated with antipsychotic monotherapy, not reflecting other researchers findings (Paton et al., 2008).

SGA use was associated with patients on oral medication (and vice versa as discussed below), antipsychotic monotherapy, having had fewer previous antipsychotics and not taking anticholinergic medication. Unexpectedly, higher doses were also associated with SGA (and again vice versa). As discussed earlier this may be because of: clearer dose ranges for the newer compared with older drugs; use of percentage maximum dose to express total dose; large differences between minimum and maximum doses for first and SGAs and poorer tolerability of older agents at higher doses. The finding of associations that occurred both when a predictor was used as an outcome and a covariate was methodologically reassuring i.e. SGA use and higher doses/oral route.

Lower use of anticholinergic medication to treat extra-pyramidal side effects would be expected when using SGAs as they are less likely to be cause movement side effects at standard doses than FGAs.

Use of the oral route of administration was associated with younger age, not having a diagnosis of schizophrenia, informal section status, fewer previous admissions, SGA use and a lower dose. As with the other outcomes younger age, informal section status and fewer previous admissions suggest a less severe and earlier stage of illness and thus a lower likelihood of non-adherence and use of depot antipsychotics (Cañas et al., 2013; Novick et al., 2010). Depot antipsychotics are reserved for long-standing cases of illness usually after oral treatments have been unsuccessful (Barnes et al., 2009; Xiang et al., 2006). At the time of data collection, depot antipsychotics were, with the exception of risperidone long-acting injection, available only as FGAs and so newer agents would be expected to be the associated with the oral route of administration. Oral antipsychotics were also associated with low doses. This may also be because depot antipsychotics, being mostly of the first generation type, have not had doses reduced as understanding of the mechanism of action of antipsychotics has developed. Flupentixol decanoate depot is a good example – the maximum dose in the UK is 400mg weekly (equivalent to approximately 8000mg of chlorpromazine equivalents (dose equivalents more than 1000mg are classed as high dose)) whereas typical clinical doses are around 30mg weekly (Taylor et al., 2015) . Patients without schizophrenia were also associated with the oral route. This association is likely to be because of the use of SGAs (available mostly as oral formulations at the time of the study) for bipolar disorder (Barnes et al., 2009).

4.4.2 Comparison with previous studies

Ethnicity was not a predictor of any of the eight outcomes but the significant limitations of the study may have resulted in negative findings. This result is similar to that found previously in analysis of this data and other smaller UK studies of inpatients. An extensive literature search of studies examining antipsychotic prescribing and ethnicity can be found in Chapter 1. Most of these studies were conducted in the US and are large database surveys so differ from this study and its predecessors. There is a large, cross-sectional UK study of antipsychotic use by ethnicity in a sample of community patients (Das-Munshi et al., 2018). As well as being from a different population to this study, the Das-Munshi paper analysed data for the five individual ethnic groups specified by the Office of National Statistics i.e. white, black, Asian, mixed, Chinese/other. It found that black patients, compared with white, were more likely to be prescribed depot antipsychotics and were less likely to be prescribed clozapine. Mixed patients were more likely than white to receive high dose antipsychotic treatment. The study was large enough (over ten thousand patients at 64 centres) to allow analysis in this way whereas this study, in order to fit models to the data, required the collapse of ethnic groups into white, black, other (Asian, mixed, Chinese/other). This distinction, as well as the differing populations are possible reasons for the differing results, notwithstanding the limitations of this study.

Previous studies have found predictors of antipsychotic polypharmacy to be anticholinergic use, male gender, poor symptom control and longer lengths of admission to hospital (Barnes & Paton, 2011). The demographic data, for example diagnosis, collected in the current study were similar to that used in other studies of antipsychotic prescribing practice in the UK (Barnes et al., 2009; Paton et al., 2008) so

results, being taken from a national sample of eight centres, can be described as broadly generalisable to the wider UK population.

Can antipsychotic prescribing be improved for all ethnicities? As described earlier quality improvement programmes can have major effects in some centres (Mace & Taylor, 2015) but the overall magnitude of change achieved is limited. Antipsychotic prescribing patterns are audited regularly and compared across UK NHS trusts (Paton et al., 2008). Those clinicians whose prescribing falls outside expected standards have to account for any differences and are expected to make improvements. So why do prescribers continue to use antipsychotics in an apparently ineffective and hazardous way? The main reason for poor prescribing is the lack of efficacy of many antipsychotics particularly when used in those with treatment-resistant illness. Clozapine is the most efficacious antipsychotic but it is underused for several reasons; patients refusal because of the need for regular full blood count monitoring owing to clozapine's haematological adverse effects; prescriber reluctance because of other severe side effects e.g. myocarditis, cardiomyopathy, pneumonia; prescribers' perception that patients on clozapine are less satisfied by this treatment; prescribers' preference for using combinations of antipsychotics; prescriber inexperience of using clozapine; concerns about clozapine's overall tolerability; patients' medical complications contra-indicating or cautioning clozapine use and prescribers worries about erratic compliance requiring re-titration (Gee et al., 2014; Nielsen et al., 2010; Taylor et al., 2000). The usual recommendation is that clozapine should be started after the failure (in response to or tolerability of) of two different antipsychotics. Delays in initiation are, on average, four years (Howes et al., 2012). Nonetheless providing support and expertise to prescribers when starting or re-challenging clozapine are

effective in improving prescribing rates (Gee et al., 2014; Meyer et al., 2015). Alongside this, development of specialist services to initiate and continue clozapine can also ensure earlier use. Management of clozapine's many side effects, even the serious haematological ones, is also possible enabl1ing patients to remain on treatment (Meyer et al., 2015; Taylor et al., 2015) and reduce their length of stay in hospital (Gee et al., 2016).

4.4.3 LIMITATIONS

Cases with complete data were used for analysis because of the large sample size. Simple single imputation methods (e.g. mean, last observation carried forward) may cause biased results because of small standard errors and do not account for the uncertainty of missing values. Even using multiple imputations can produce misleading results e.g. the QRISK study found no relationship between cholesterol and cardiovascular risk until completion of a complete case analysis (Sterne et al., 2009) and there is little research into calculating multiple imputations for binary or categorical data. Nonetheless errors can be avoided if results are carefully checked and appropriate imputation methods are used.

Using complete cases for analysis may not always be biased if the missing data occur only in an outcome variable that is measured once in each individual, if all variables associated with missing outcome data can be included as covariates and if missing data in predictor variables are unrelated to outcome. This applied to the data used in this analysis if variables were not included that were derived from the outcomes. Notwithstanding this, complete case analysis can be biased unless data are MCAR. The data were MAR not MCAR because missing data were distributed in one or more

subsamples (i.e. centres with poorer complete data collection e.g. North East London, Manchester). Data were analysed previously as MAR to allow multiple imputations (see Chapter 2) and the six variables with the most missing data (accounting for almost 70% of total missing data) were education, weight, duration of illness, length of treatment with current antipsychotic, previous treatment with current antipsychotic, and number of previous antipsychotic treatments. For the final linear models, of these variables only weight was a significant predictor of dose and none of these variables were significant predictors of cost. For the logistic final models, of these variables only number of previous antipsychotic treatments was a significant predictor of type of antipsychotic in the final model and none were significant predictors of polypharmacy prescribed, polypharmacy administered and route of administration.

As in previous analyses the regression models had poor predictive power and the extent of the effects were mostly small. Numerous variables were collected that could have affected the outcomes, using both previous research and clinical experience to collate the covariates, but this added to the complexity of the models. Indeed for two outcomes, clozapine use and high dose, it was not possible to fit a model. Other researchers did not adjust their models for such a large number of confounders (see Appendix 2). The poor explanatory power of the models suggests that there are unknown or uncollected variables influencing the outcomes. The categorical variables in the models had their number of levels collapsed to reduce data complexity and allow model fit. This may have affected the results by simplifying confounders associated with outcomes.
It is also possible that the models' predictive capacity could be affected by the inclusion of too many variables i.e. overadjustment of outcomes as discussed in Sections 2.4.6 and 3.4.3. As multiple confounders were included in the models for all ethnicities data –

many more than in previous studies (see Appendix 2) but fewer than in the black and white patient analyses – this could have affected the results.

There were some variables that were not collected that other researchers found were 251associated with antipsychotic use and ethnicity - data on patients' mental state (Shi, 2007; Van Dorn et al., 2005) and reasons for antipsychotic choice. Data on patients' mental state (a CGI-S score) was collected in previous research (Connolly & Taylor, 2008). But given the cross-sectional nature of the study, this score was collected on the day of data collection not at the time of prescribing of the antipsychotic so was of limited usefulness as what is important is the severity of illness before the treatment becomes effective. This analysis used complete cases whereas previous analyses had used multiple imputations to replace missing data. This may have affected the models' reliability however those from the previous analysis also explained only limited variability.

As in Chapters 2 and 3, classification of ethnicity using the Office of National Statistics grouping masked the heterogeneity of the people in these categories and could have affected the results. Furthermore this analysis collapsed the ethnicity groups, for statistical reasons, from five (white, black, Asian, mixed, Chinese/other) to three (white, black, other) further eroding group heterogeneity and very possibly the results.

All variables collected in the study were not included in the regression models for all outcomes in this analysis (as they were for the black and white patient analysis in Chapters 2 and 3). Only those variables associated with each outcome were included as listed in Tables 36 and 39. This may have affected which variables were associated with each outcome, for example age was associated with prescribed polypharmacy and route

of administration but not administered polypharmacy as in previous analyses in Chapter 2.

This study did not find differences in the prescribing of antipsychotics by ethnicity in a sample including patients of all ethnicities, but there were significant limitations as detailed above. Given the shortcomings of this and the studies in Chapters 2 and 3 plus the feedback from prescribers about earlier studies of antipsychotics and ethnicity, an investigation of theoretical prescribing intention for black or white patients allowed further investigation, using a different research design, of the prescribing of antipsychotics by ethnicity.

4.5 CONCLUSIONS

Ethnicity did not affect prescribing of antipsychotics for any of the outcomes examined when adjusted for confounders but the significant limitations of the study may have resulted in negative findings. Higher doses and combinations of antipsychotics were used for patients who were detained under the Mental Health Act, had longer lengths of admission, more previous admissions, of larger weight, not taking clozapine, using a depot antipsychotic and being assessed as poorly compliant.

Using the percentage maximum dose method of expressing dose may have allowed older agents to appear more favourably. As reported in other studies polypharmacy and high doses are linked. Newer SGAs were not associated with anticholinergic medicine use because of their lower risk of EPSE and were used for patients who had been treated with fewer previous antipsychotics. Oral medicines were used for patients who were younger, not detained, did not have schizophrenia, had had fewer previous admissions, on a SGA and taking a lower dose.

CHAPTER 5 DOES ETHNICITY AFFECT PRESCRIBING FOR ACUTE PSYCHOSIS? EVALUATION BY CASE VIGNETTE

5.1 INTRODUCTION

People from ethnic minorities, particularly black patients, are disproportionately represented in mental health services (Care Quality Commission, 2010), more likely to be admitted to hospital and sectioned under the Mental Health Act than white patients (Care Quality Commission, 2010; Morgan et al., 2006). There have also been a number of high-profile deaths of black patients in psychiatric services (Norfolk Suffolk & Cambridgeshire Strategic Health Authority, 2003; Prins, 1993) that have given rise to charges of institutional racism in UK mental health services (McKenzie & Bhui, 2007). The concern is that this racism is manifested in different prescribing practices for black people.

Indeed prescribing of antipsychotics differs by ethnicity in some countries, especially the US. Studies show black patients are more likely to receive higher doses, FGAs and greater numbers of antipsychotics than white patients (Diaz & De Leon, 2002; Kreyenbuhl et al., 2003; Taylor, 2004).

Studies from the UK have not shown major differences in antipsychotic prescribing between black and white patients (Connolly et al., 2007; Connolly & Taylor, 2008). These studies have examined outcomes including dose, type of antipsychotic, number of antipsychotics prescribed, route of administration, clozapine use and costs of antipsychotics in large, multicentre studies. Different health care systems, decline in and

awareness of racism and a multi-ethnic mental health workforce may account for these differences (Goldacre et al., 2004).

After publication of the study examining antipsychotic prescribing in black and white patients, the results were presented and discussed with health care professionals. The informal feedback received from ethnic minority prescribers, rather than welcoming the results, was that the findings of previous studies were flawed. Individual prescribers stated that they purposefully used higher doses for black patients as these patients were more severely unwell on admission than white patients often because of delays in accessing mental health services. Illness severity was not collected as a measure in the study described in Chapter 2 as had been done in an earlier investigation (Connolly & Taylor, 2008). Moreover the AESOP study examined duration of untreated psychosis by ethnicity – a proxy measure of illness severity. It did not find that black patients compared with white had a longer duration of untreated psychosis (Morgan et al., 2006). .

Given the nature of this informal feedback and the limitations of previous studies, the legitimacy of these reports could be tested, using a different research design to studies in Chapters 2, 3 and 4, through a theoretical study examining attitudes of prescribers to prescribing by ethnicity. This was carried out by developing a patient case vignette capturing the different ethnicities and then requesting prescribers to choose antipsychotic treatment(s) and dose(s) so that a comparison could be made on an intention-to-treat basis.

5.2 METHOD

A case vignette (see Appendix 16), prescriber demographic data form (Appendix 17) and study explanatory letter (Appendix 18) were sent to all medical prescribers in the South London and Maudsley NHS trust. The case study was produced using several methods - examining vignettes from previous studies (Clark & Rowe, 2006; Lewis & Appleby, 1988; Lewis et al., 1990), contacting authors of previous studies where the case was not published as part of the paper (Minnis et al., 2001), personal experience of common clinical scenarios and consulting with colleagues as to the validity and suitability of the case. Half of the prescribers for each grade of staff (foundation year (FY1-2), core trainee (CT1-2), speciality registrar (StR 1-6) and consultant) were emailed the case study where the ethnicity of the patient was white and the other half where the ethnicity was black. This was the sole difference between the vignettes. Replies could be made by email or anonymously in the post. Those who did not respond were sent a final reminder email 2 weeks later.

The case study asked only two questions; which antipsychotic(s) would you prescribe for this patient and what dose(s) would you use? The explanatory letter asked prescribers to complete a survey of antipsychotic prescribing and stated that the reasons for the study could not be revealed as this would nullify the results. The case study was tested before distribution to ensure suitability and that it could be easily completed and understood.

5.2.1 ETHICAL COMMITTEE APPROVAL

The Health Research Authority's guidance (Health Research Authority, 2014) on defining research was used to determine if the study was research, clinical audit or a

service evaluation. This study was defined as 'not research' (Appendix 19) and as such approval was obtained from the South London and Maudsley NHS trust Drugs and Therapeutics committee.

5.2.2 Statistical Analysis

The outcomes analysed were: total percentage maximum dose (calculated as dose divided by maximum BNF dose (British Medical Journal Group and Pharmaceutical Press, 2014), multiplied by 100); percentage maximum dose for 1st, 2nd, 3rd antipsychotic choice; high dose (more than 100% of BNF maximum dose); type of antipsychotic (FGA or SGA); route of administration (oral or IM) and antipsychotic polypharmacy (being prescribed more than one antipsychotic concurrently). Prescribers' demographic data were summarised using descriptive statistics and then inferential statistics were used for each outcome by case ethnicity. Relationships between outcomes and prescriber demographic data were explored using t-tests and ANOVA for continuous and chi-squared for categorical outcomes. Some continuous variables were not normally distributed and so were transformed and in one case (age of prescriber), put into discrete categories to allow statistical interpretation. All analyses were performed using IBM SPSS software.

5.3 Results

5.3.1 Study Population

The contact details for prescribers in the trust were obtained and emails sent to all 784 with an explanatory letter, a demographic data form and the case vignette for completion. The total number of completed replies received was 123 (15.7%), of which 120 (97.6%) were returned by email and 3 (2.4%) anonymously in the post. Clinical and demographic characteristics of prescribers are detailed in Table 45 and 46. The case

vignettes returned were approximately equal for both ethnicities i.e. those where the patient was described as white (n= 63 (51.2%)) and black (n=60 (48.8%)).

Respondents often listed several possible antipsychotic treatment options in reply to the case study questions, for example olanzapine or aripiprazole or quetiapine or risperidone. These were labelled in the order written as antipsychotic 1 or antipsychotic 2 or antipsychotic 3 or antipsychotic 4 for each outcome i.e. percentage maximum dose and type of antipsychotic.

TABLE 45 CATEGORICAL CLINICAL AND DEMOGRAPHIC CHARACTERISTICS OF PRESCRIBERS

Demographic	**Category**	**Frequency n = 123 (%)**	**Missing Cases (%)**
Gender	Male	76 (61.8)	0
Grade	Consultant	50 (40.6)	1 (0.8)
	Speciality Trainee	42 (34.1)	
	Core Trainee	12 (9.8)	
	Foundation Trainee	18 (14.6)	
Ethnicity	White	88 (71.5)	2 (1.6)
	Asian	18 (14.6)	
	Black	8 (6.5)	
	Mixed	4 (3.3)	
	Other	2 (1.6)	
	Chinese	1 (0.8)	
Case Ethnicity	White	63 (51.2)	0

TABLE 46 CONTINUOUS CLINICAL AND DEMOGRAPHIC CHARACTERISTICS OF PRESCRIBERS

Demographic	**Mean (Range)**	**Missing Cases (%)**
Age (years) n = 115	39.7 (25-65)	8 (6.5)
Percentage maximum antipsychotic 1, n=122*	42.66 (0.63-100)	0
Percentage maximum antipsychotic 2, n=28	52.04 (3.13-100)	2 (1.6)
Percentage maximum antipsychotic 3, n=12	46.69 (6.25-75)	1 (0.8)
Total percentage maximum, n=120	49.32 (0.63 -175)	3 (2.4)

* 1 case drug chosen not an antipsychotic

5.3.2 OUTCOMES

Descriptive data for each of the categorical outcomes (high dose, type, polypharmacy and route) are listed in Table 47 and continuous outcomes (total percentage maximum dose, percentage maximum dose for antipsychotic 1, 2 and 3) in Table 48. Oral SGA were the most commonly prescribed type of antipsychotic and most respondents avoided using high doses or combinations of antipsychotics.

TABLE 47 OUTCOMES OF CASE VIGNETTE

Outcome	**Category**	**Frequency n=123 (%)**	**Missing Cases**
Type of antipsychotic 1	SGA	117 (95.1)	0
	FGA	5 (4.1)	
	Not an antipsychotic	1 (0.8)	
Type of antipsychotic 2	SGA	23 (18.7)	0
	FGA	3 (2.4)	
	Not an antipsychotic	2 (1.6)	
	None	95 (77.2)	
Type of antipsychotic 3	SGA	12 (9.8)	0
	FGA	1 (0.8)	
	None	110 (89.4)	
Type of antipsychotic 4	SGA	1 (0.8)	0
	FGA	0	
	None	122 (99.2)	
Polypharmacy (more than one antipsychotic prescribed)	No	111 (90.2)	0
High dose (more than 100% BNF maximum)	No	114 (92.7)	3 (2.4)
Route	Oral	111 (90.2)	0
	IM	1 (0.8)	
	Oral or IM	11 (8.9)	

5.3.2.1 TOTAL DOSE (PERCENTAGE MAXIMUM DOSE)

Percentage maximum dose for antipsychotic 1 and total percentage maximum were broadly normally distributed (data were explored through P-P plots, histograms, Levene's and Kolmogorov-Smirnov tests (Field, 2013)).

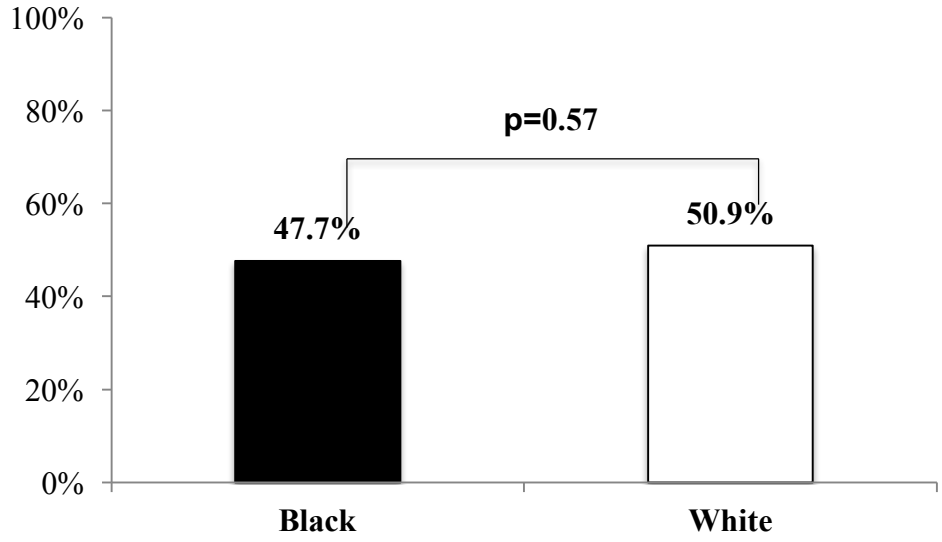
The mean total doses for black and white patients were 47.7% and 50.9% respectively (Figure 13). There were no significant differences in total dose of antipsychotic by case ethnicity (p=0.567) (see Table 48).

TABLE 48 TOTAL DOSE AND CASE ETHNICITY

Total dose (% maximum)	**Case Ethnicity**	**n**	**Mean (% maximum)**	**t**	**P**
Antipsychotic 1	Black	60	41.82	0.481	0.632
	White	62*	43.46		
Antipsychotic 2	Black	11*	53.31	-0.196	0.846
	White	15*	51.10		
Antipsychotic 3	Black	4	62.50	-1.804	0.101
	White	9	38.78		
Total Dose	Black	59	47.69	0.575	0.567
	White	61	50.89		

* 1 case drug chosen not an antipsychotic

FIGURE 13 TOTAL DOSE (PERCENTAGE MAXIMUM) BY CASE ETHNICITY

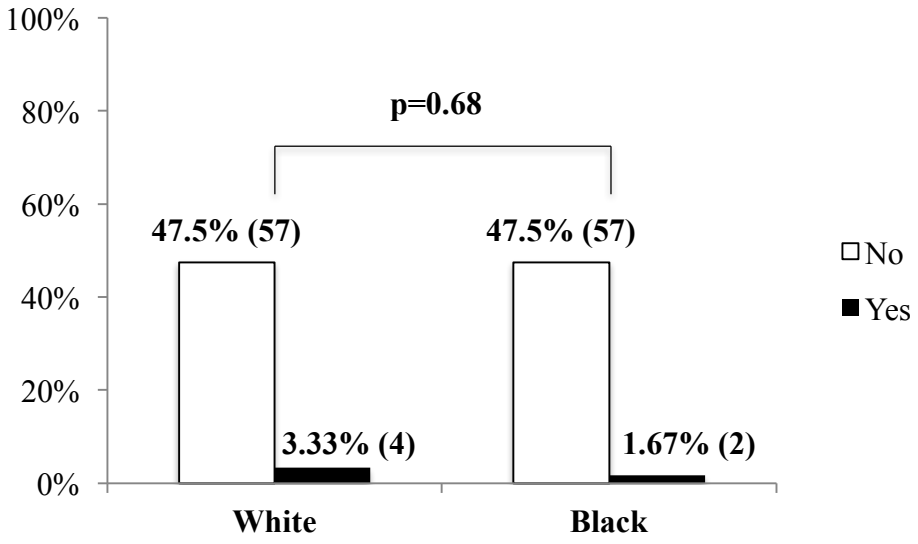


The percentage maximum dose for antipsychotic 2 and 3 were not normally distributed, even after transformation. A 2-sided t-test is robust enough to allow use for non-normal variables if the sample size is large (Lumley et al., 2002). There were no significant differences in dose of antipsychotic 1, 2 or 3 by case ethnicity (see Table 48).

5.3.2.2 HIGH DOSE

There were no differences in high dose prescribing (p=0.68, Figure 14) by case ethnicity.

FIGURE 14 HIGH DOSE ANTIPSYCHOTIC BY CASE ETHNICITY

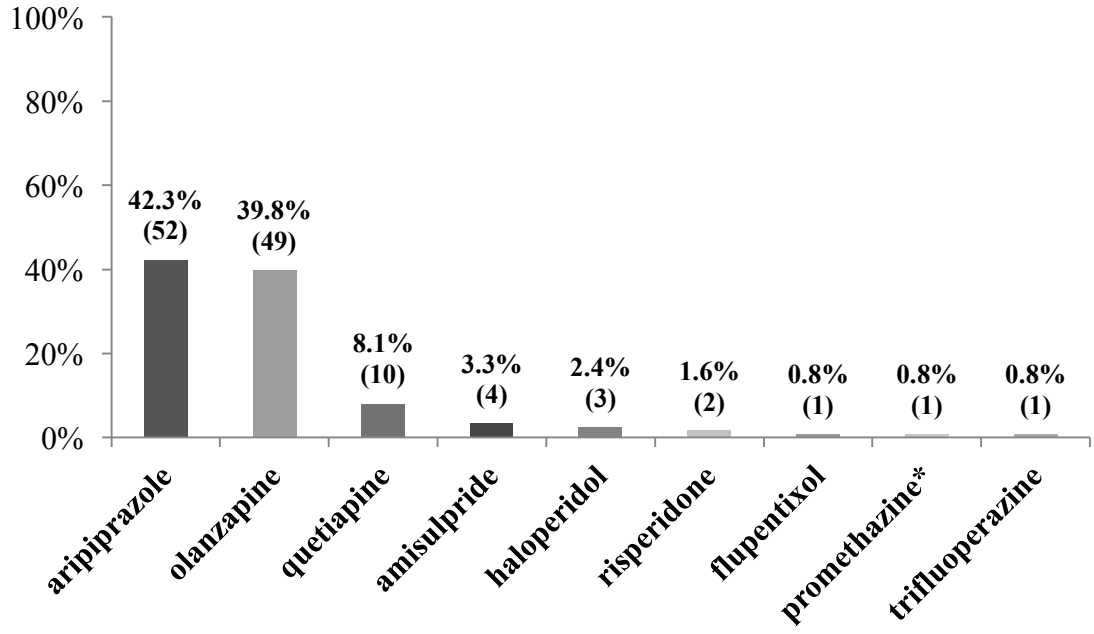


5.3.2.3 CHOICE AND TYPE OF ANTIPSYCHOTIC

The most frequently chosen antipsychotics were aripiprazole then olanzapine, accounting for 82.1% of choices (Figure 15). There were no differences by case ethnicity in type (FGA or SGA) of antipsychotic 1 (Figure 16), antipsychotic 2 or antipsychotic 3 (Tables 49 and 50).

Fisher's exact test was conducted on choice of antipsychotic 1, 2 and 3 to overcome the problem of small cell sample sizes. Chi-squared tests were not possible for choice of antipsychotic 1, 2, 3 and high dose as more than 20% of some cells had expected frequencies of less than five cases. This invalidated the test as it ceased to approximate to the chi-squared distribution.

FIGURE 15 CHOICE OF ANTIPSYCHOTIC BY CASE ETHNICITY (1ST ANTIPSYCHOTIC LISTED)



* not an antipsychotic
( ) frequency

FIGURE 16 TYPE OF ANTIPSYCHOTIC 1 BY CASE ETHNICITY

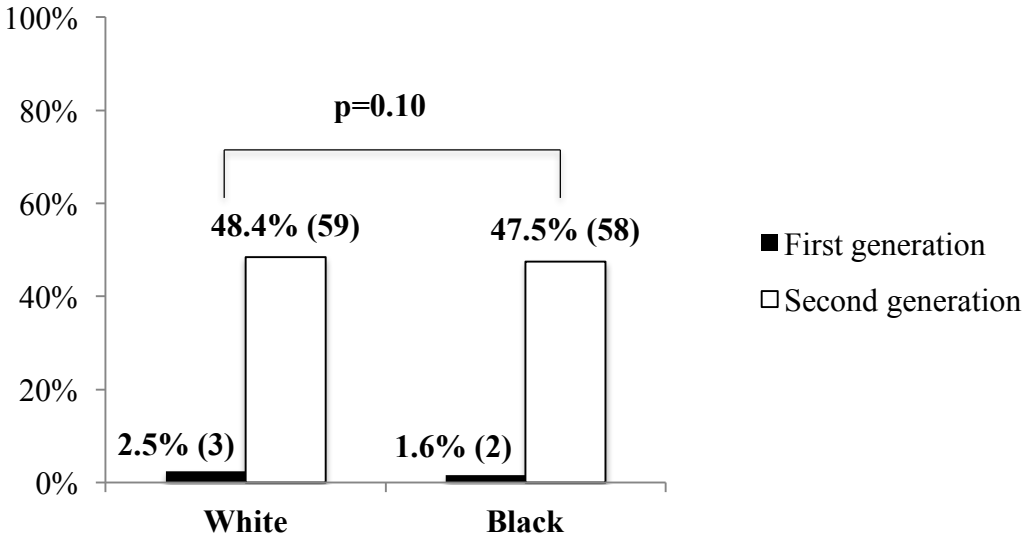


TABLE 49 TYPE OF ANTIPSYCHOTIC 2

Antipsychotic Choice 2	Case Ethnicity		Total
	White	Black	
FGA	3	0	3
SGA	12	11	23
Not an antipsychotic	1	1	2
Total	16	12	28

Fishers exact test 0.367 (exact significance 2-sided)

TABLE 50 TYPE OF ANTIPSYCHOTIC 3

Antipsychotic Choice 3	Case Ethnicity		Total
	White	Black	
FGA	1	0	1
SGA	8	4	12
Total	9	4	13

Fishers exact test 1.000 (exact significance 2-sided)

5.3.2.4 ANTIPSYCHOTIC POLYPHARMACY

There were no differences in antipsychotic polypharmacy (p=0.37, Figure 17) by case ethnicity. Table 51 lists the combinations chosen.

FIGURE 17 POLYPHARMACY BY CASE ETHNICITY

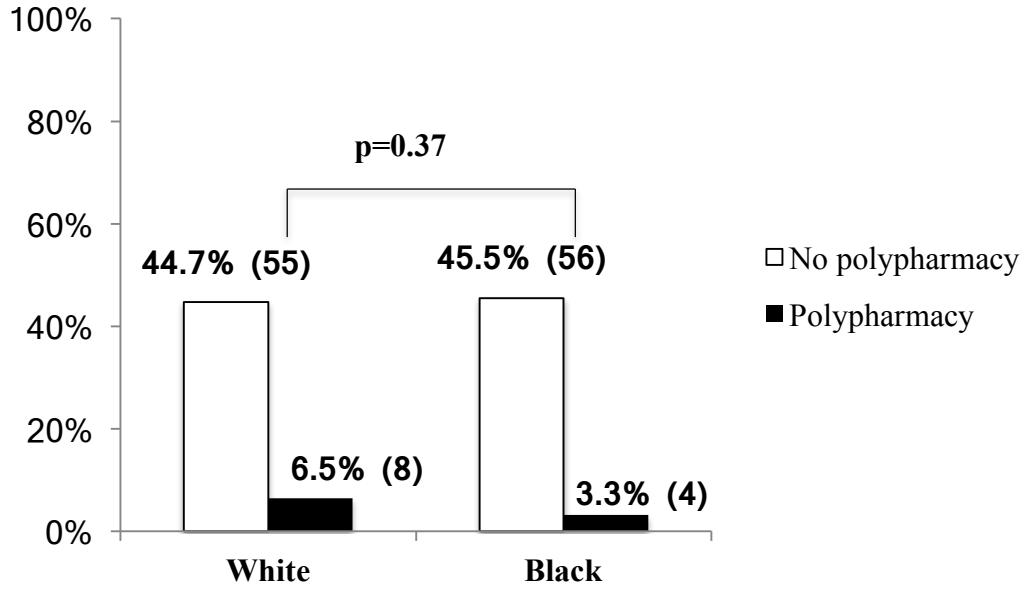


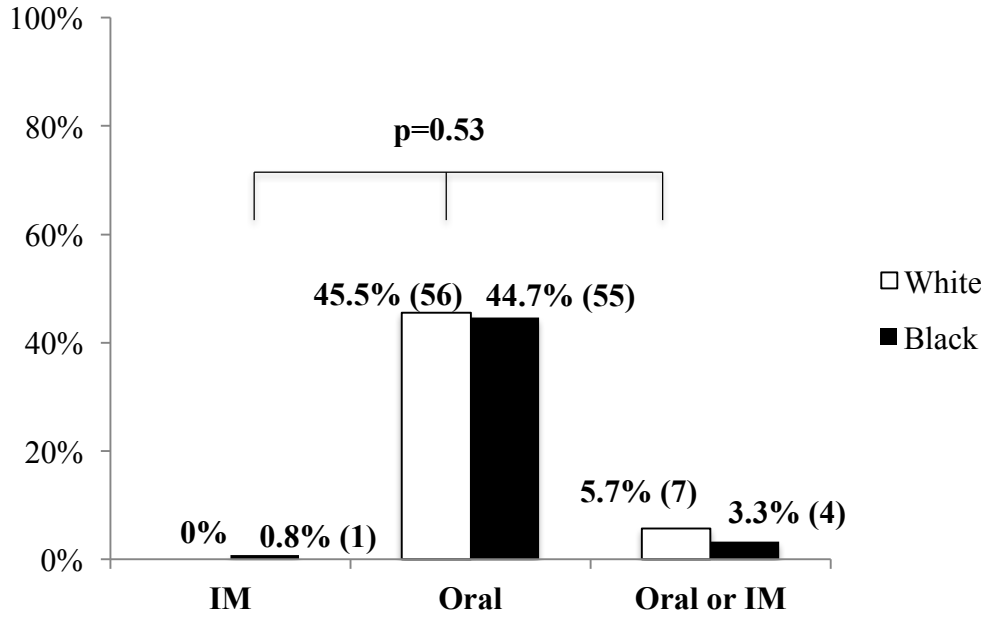
TABLE 51 ANTIPSYCHOTIC POLYPHARMACY COMBINATIONS

Polypharmacy combinations	**N**	**Ethnicity**
Olanzapine and aripiprazole	2	1 black, 1 white
Olanzapine, aripiprazole and quetiapine	2	1 black, 1 white
Olanzapine, aripiprazole, quetiapine and amisulpride	1	1 black
Olanzapine, aripiprazole and amisulpride	1	1 white
Olanzapine, aripiprazole and trifluoperazine	1	1 white
Olanzapine, aripiprazole and risperidone	1	1 white
Olanzapine, aripiprazole and haloperidol	1	1 white
Haloperidol and zuclopentixol decanoate	1	1 white
Aripiprazole and quetiapine	2	1 black, 1 white
Total	**12**	**4 black, 8 white**

5.3.2.5 ROUTE OF ADMINISTRATION

There were no differences in route of administration (p= 0.53, Figure 18) by case ethnicity.

FIGURE 18 ROUTE OF ANTIPSYCHOTIC BY CASE ETHNICITY



5.3.3 PRESCRIBER VARIABLES AND OUTCOMES

Each prescriber variable (age, gender, grade of staff and ethnicity) was examined to determine if associated with the outcomes (total dose, high dose, polypharmacy, type and route).

Age was not normally distributed. All transformations were applied (natural log, 1/square root, reciprocal, square root, square, cube) but age was still unable to achieve normality.

5.3.3.1 TOTAL DOSE

Age was not normally distributed but three discrete categories were evident. It was divided into these 3 categories (32 or less, 33-44, 45 or more). Mid-aged (33-44 year olds) prescribers were more likely to use higher doses (p=0.01). Gender, grade of staff and prescriber ethnicity were not significantly associated with total dose (see Table 52).

TABLE 52 TOTAL DOSE AND PRESCRIBER VARIABLES

Total Dose	**t**	**p**	**95% Confidence Interval**	
			Lower	**Upper**
Gender	-0.707	0.48	-15.32	7.26
Grade (Consultant or not)	-1.116	0.27	-17.66	4.93
Ethnicity (white or not white)	0.464	0.64	-9.64	15.54

5.3.3.2 HIGH DOSE

As with total dose, mid-aged prescribers were more likely to prescribe high doses (p=0.04). Gender, grade and prescriber ethnicity were not significantly associated with high dose (see Table 53).

TABLE 53 HIGH DOSE AND PRESCRIBER VARIABLES

Prescriber variable	**High Dose**		**Total**	**p**
	No	**Yes**		
Age				
32 or less	37	0	37	0.04
33 to 44	35	5	40	
45 or more	34	1	35	
Total	106	6	112	
Gender				
Male	69	4	73	1.00
Female	45	2	47	
Total	114	6	120	
Grade				
Consultant	46	2	48	0.93
Speciality Trainee	39	3	42	
Core Trainee	12	0	12	
Foundation Trainee	16	1	17	
Total	113	6	119	
Ethnicity				
White	82	4	86	0.68
Asian	16	1	17	
Black	7	1	8	
Mixed	4	0	4	
Other	2	0	2	
Chinese	1	0	1	
Total	112	6	118	

5.3.3.3 TYPE OF ANTIPSYCHOTIC

No association was found between any prescriber variables for type of antipsychotic outcomes (see Table 54).

TABLE 54 TYPE OF ANTIPSYCHOTIC AND PRESCRIBER VARIABLES

Prescriber variable	**Type**			**Total**	**p**
	FGA	**SGA**	**Not an antipsychotic**		
Age					
32 or less	0	37	0	37	0.31
33 to 44	3	38	0	41	
45 or more	2	34	1	37	
Total	5	109	1	115	
Gender					
Male	3	72	1	76	1.00
Female	2	45	0	47	
Total	5	117	1	123	
Grade					
Consultant	3	47	0	50	0.47
Speciality Trainee	2	40	0	42	
Core Trainee	0	12	0	12	
Foundation Trainee	0	17	1	18	
Total	5	116	1	122	
Ethnicity					
White	2	85	1	88	0.393
Asian	2	16	0	18	
Black	1	7	0	8	
Mixed	0	4	0	4	
Other	0	2	0	2	
Chinese	0	1	0	1	
Total	5	115	1	121	

5.3.3.4 ANTIPSYCHOTIC POLYPHARMACY

Mid-aged prescribers were more likely to prescribe more than one antipsychotic concurrently (p= 0.001). Gender, grade and prescriber ethnicity were not significantly associated with polypharmacy (see Table 55).

TABLE 55 POLYPHARMACY AND PRESCRIBER VARIABLES

Prescriber variable	**Polypharmacy**		**Total**	**p**
	No	**Yes**		
Age				
32 or less	37	0	37	0.001
33 to 44	31	10	41	
45 or more	35	2	37	
Total	103	12	115	
Gender				
Male	70	6	76	0.53
Female	41	6	47	
Total	111	12	123	
Grade				
Consultant	44	6	50	0.69
Speciality Trainee	37	5	42	
Core Trainee	12	0	12	
Foundation Trainee	17	1	18	
Total	110	12	122	
Ethnicity				
White	83	5	88	0.06
Asian	14	4	18	
Black	6	2	8	
Mixed	3	1	4	
Other	2	0	2	
Chinese	1	0	1	
Total	109	12	121	

5.3.3.5 ROUTE OF ADMINISTRATION

No association was found between any prescriber variables for route of administration outcomes (Table 56).

TABLE 56 ROUTE OF ADMINISTRATION AND PRESCRIBER VARIABLES

Prescriber variable	**Route**			**Total**	**p**
	IM	**Oral**	**Oral or IM**		
Age					
32 or less	0	35	2	37	0.22
33 to 44	1	38	2	41	
45 or more	0	31	6	37	
Total	1	104	10	115	
Gender					
Male	1	67	8	76	0.71
Female	0	44	3	47	
Total	1	111	11	123	
Grade					
Consultant	1	44	5	50	0.87
Speciality Trainee	0	39	3	42	
Core Trainee	0	12	0	12	
Foundation Trainee	0	16	2	18	
Total	1	111	10	122	
Ethnicity					
White	1	83	4	88	0.10
Asian	0	15	3	18	
Black	0	7	1	8	
Mixed	0	3	1	4	
Other	0	1	1	2	
Chinese	0	1	0	1	
Total	1	110	10	121	

5.4 Discussion

5.4.1 Main Findings

Antipsychotic prescribing did not differ between black and white ethnicity when tested using a theoretical case vignette method. This study, unlike others previously, measured several outcomes of antipsychotic use including dose, antipsychotic combination, type and route of administration. The significant limitations of the study may have resulted in negative findings.

Most prescriber variables were not associated with any of the outcomes. Prescribers aged between 33 and 44 years were more likely to prescribe larger total doses, high doses and more than one antipsychotic concurrently. Results may be influenced by the greater experience and thus prescribing confidence in this age group but the expectation would be that this experience would result in better prescribing.

5.4.2 Comparison With Previous Studies

Other studies have used similar methods to determine if treatment of mental ill-health differs by ethnicity. Lewis and colleagues (Lewis et al., 1990), in their challengingly titled study 'Are British psychiatrists racist?', used a case study of a black or white, male or female patient to measure effects of gender and ethnicity on a series of statements about the assessment, management and treatment of the patient in the case. These included three medication outcomes about antipsychotics, antidepressants and treatment compliance. White patients were rated by psychiatrists as significantly more likely than black to need 'neuroleptic treatment' but there were no differences by ethnicity for 'antidepressant treatment not indicated' and 'unlikely to comply'. Ten years later Minnis and colleagues (Minnis et al., 2001) repeated the study in a similar

fashion using a case vignette accompanied by a photograph of a white or black man. As Lewis and colleagues had found before, white patients were more likely to have 'neuroleptic drug treatment indicated' than black. So previous studies using similar methodology found, as did this study, that black patients were not judged more likely to need antipsychotic treatment.

5.4.3 LIMITATIONS

The case vignette design of this study was similar to that used in two previous studies as it contained a comparable level of detail but differed in that the patients in the earlier studies had first episode psychotic symptoms not a psychotic relapse. A relapse in psychosis may be more likely to be treated with more than one antipsychotic or a high dose compared with first episode psychosis where patients are usually antipsychotic naive and treated with a single agent.

The return rate for questionnaires was lower than achieved by other studies using similar methods - 15.7% compared with 59% (Minnis et al., 2001) and 73% (Lewis et al., 1990). The survey was emailed to prescribers, this allowed them to be easily ignored or quickly deleted. The questionnaires should not have become 'junk' email as they were sent from an internal email address which the system would recognise as legitimate. Prescribers receive large volumes of unsolicited email perhaps accounting for the low response rate. Moreover questionnaires sent out by email usually receive responses much lower than those sent out on paper. Despite this, average email return rates are around 33% (Nulty, 2008), much higher than reached by this study. Survey platforms such as Survey Monkey (www.surveymonkey.com, (Nair & Adams, 2009)) are a common way of distributing questionnaires electronically. They are very user-

friendly allowing rapid completion and return of information and even, with some packages, analysis of results. This approach was not used because of financial constraints. Respondents to the survey had to complete two documents (the questionnaire and demographic form), save them and then email them back. Indeed some prescribers' initial replies were blank as they had not saved the completed forms. Anonymous replies could be sent through the post but this required several additional steps in the process perhaps accounting for the low postal return rate. The prescribers contacted with the questionnaire were largely unknown so there was a lower motivation to reply than if surveying colleagues (Nulty, 2008). A reminder email did elicit further responses. This is the third such study of its kind so a degree of questionnaire fatigue may have set in, reducing the return numbers. The prescribers' ethnicity was requested directly whilst previous studies (Lewis et al., 1990; Minnis et al., 2001) either did not collect any respondent ethnicity data or collected indirect indicators i.e. medical school of graduation. This was due to a concern that inquiring about ethnicity would reveal the principal reason for the study and consequently affect outcome. Despite this, a small proportion (1.7% (Minnis et al., 2001)) of their respondents still guessed correctly or implied they had guessed by replying but refusing to participate (5.2% (Lewis et al., 1990)).

Some respondents may have known or suspected the reason for the survey but none informed me that they had deduced the purpose. Understandably (given the explanatory letter) many asked to be informed of the study's intention when collection was complete. Others were worried that the survey was some sort of prescribing test set by the trust to measure prescribing competence and were anxious to provide 'correct answers'. Despite this level of suspicion the prescribers' ethnicity (despite the risks of

study unmasking) was still requested to test comments by ethnic minority prescribers that they purposely prescribed differently by ethnicity.

As in earlier chapters, classification of prescriber ethnicity using the Office of National Statistics groups masked the heterogeneity of the people in these categories and could have affected the results. Using a greater number of classifications of ethnicity may have resulted in a different outcome i.e. prescriber ethnicity could have been associated with dose, high dose, type of antipsychotic, polypharmacy or route of administration.

A small amount of prescriber demographic data variables were missing. Age was most likely to be omitted then ethnicity and lastly grade of staff. It may have been that some of this information was personally sensitive or simply missing because of lack of attention by those completing the form. Antipsychotic polypharmacy results may have been due to prescribers not indicating on the questionnaire that their drug choices were alternatives to each other not additions.

5.5 Conclusions

Despite comments from ethnic minority prescribers rebutting the results of previous studies, this theoretical study of prescribers' attitudes to antipsychotic prescribing by ethnicity yielded supporting results. That is that antipsychotic prescribing, when tested in both clinical and hypothetical studies, did not differ for black and white ethnicities. However it is important to note that the significant limitations of the study may have resulted in negative findings.

CHAPTER 6 SUMMARY, CONCLUSIONS AND RECOMMENDATIONS

6.1 SUMMARY OF THESIS AND CONCLUSIONS

Prescribing of antipsychotics in patients of different ethnicities has been the focus of this thesis. The results of a multicentre study examining these issues for black and white patients separately, all ethnicities combined and the effects of each centre on study outcomes have been evaluated and reported. As well as this medical prescriber attitudes to prescribing by ethnicity using a case vignette have been explored. The results of these investigations did not find differences in prescribing by ethnicity in either real-life (clinical) and simulated (theoretical) circumstances. That is not to say that some centres do not have poorer prescribing by ethnicity that requires remedial action, but overall total data analysis showed no important differences. The significant limitations of the studies may have resulted in negative findings.

Defining ethnicity can be difficult, and sometimes controversial. This is because few people have a single genetic identity, ethnicity is a fundamental part of most people's individuality and the history of abuse by ethnicity. The description of ethnicity has developed from the collection of merely factual data i.e. country of birth or nationality to more complex descriptions encompassing heritage and national identity. Inevitably compromises are made to allow categorisation, masking heterogeneity of people in these categories.

Ensuring all ethnic groups are involved in research studies is important for the generalisability of results and fairness of treatment. Research study abuses such as the Tuskegee syphilis study (Centers for Disease Control and Prevention, 1997) have

affected trust in researchers and greater efforts to engage and recruit ethnic minorities are, finally, being recognised as important in study outcomes. Accurate measurement of ethnicity is important to ensure health services are equitable and the self-assigned systematic and mandatory collection of ethnicity data by the UK NHS has allowed this to occur. Poverty and health inequality are strongly associated and ethnic minorities are overrepresented in lower socioeconomic groups. But not all health inequality within and between ethnic groups can be attributed to social groupings.

Treatment of mental illness differs for ethnic minorities. Many reports, investigations, public enquiries and surveys have been conducted documenting differences in referral to specialist mental health services, admission rates to hospital, detention under the Mental Health Act and seclusion whilst in hospital. This is particularly so for black patients compared with white. Could this be because rates of psychosis and schizophrenia are much higher for black patients? Differences in symptom expression and presentation, social factors, routes of admission to hospital and racism are all suggested causes. Whatever the social and environmental causes, there is still some way to go to understand these ethnic variations.

Research, predominantly from the US, showing differences in prescribing of antipsychotics for ethnic minorities raised concern in the UK that there may be prejudicial prescribing of antipsychotics. These suggested differences included use of high doses, more frequent use of older drugs and depot formulations, particularly for black compared with white patients. Ethnic groups may metabolise antipsychotics differently because of enzymatic genetic polymorphism. However, with the possible exception of Asian peoples, an individual's own metabolising capacity is probably a

more important factor than their ethnicity alone. Nevertheless patients, carers and official reports demanded investigation into any potential differences in prescribing of antipsychotics by ethnicity.

The multicentre study of antipsychotic prescribing of inpatients in eight UK mental health trusts conducted in this research programme did not find differences by ethnicity in dose, high dose, polypharmacy prescribed and polypharmacy administered, type of antipsychotic, route of administration, clozapine use and cost of antipsychotic treatment. However there were significant limitations as described in detail in each chapter and Section 6.2. This study fulfilled calls from reports into mental health services and ethnicity to investigate prescribing practices in the UK because of differences found in antipsychotic prescribing and ethnicity research studies (see Table 3). Most concerns about prescribing have been in black compared with white patients. These two ethnic groups have the largest proportions of inpatients in UK NHS mental health trusts and so, for these reasons, this was the first analysis. The outcomes were adjusted for over twenty different confounding factors and analysed in several ways (primary outcome-complete cases, complete cases, black compared with white ethnicity (Chapter 2), including centre as a confounder (Chapter 3), all ethnicities (Chapter 4)). Differences were not found by ethnicity in these adjusted analyses. However higher order grouping into broad ethnic categories can mask the heterogeneity of people and may conceal important differences in the results.

Individual centre analysis for black and white patients (see Chapter 3) developed the Chapter 2 study by investigating variation in prescribing practice by centre to determine if prescribing practice differs between NHS Trusts not just within these ethnic groups.

This study did reveal differences in prescribing by ethnicity, particularly for one centre. These effects included higher doses, polypharmacy, greater use of FGAs and higher costs. For some of these outcomes it was not possible to adjust results for potential confounders because of small sample sizes and missing data. All centres where differences were found, whether adjusted or not, were informed of their results so enabling them to investigate reasons for any differences and make changes where needed.

Analysis of data for all ethnicities in Chapter 4 develops the studies in Chapters 2 and 3 by investigating a larger sample (through the inclusion of proportionally smaller ethnic groups) to discover if prescribing varies by these ethnicities. It did not find differences in antipsychotic prescribing although there were significant limitations. The study did find many variables associated with the study's outcomes. Higher doses and combinations of antipsychotics were used for patients who were likely to have a more severe illness i.e. were detained, had longer lengths of admission and more previous admissions. Larger weight, not taking clozapine, using a depot antipsychotic and being poorly compliant with medication were also associated with these outcomes. The use of FGAs was associated with lower doses possibly because of the use of the percentage maximum dose method of expressing dose results. As expected and reported in previous studies, polypharmacy and high doses were closely related. SGAs were used for patients who had taken fewer previous antipsychotics and did not take (or need) anticholinergic medicines. Oral medicines were used for patients who were probably less chronically ill i.e. younger, not detained, had had fewer previous admissions, were taking a lower dose, did not have schizophrenia and taking a SGA. Some of these relationships were unexpected, for example lower doses and FGA, but most could be hypothesised rationally.

After publication of previous studies on antipsychotic prescribing and ethnicity, some ethnic minority prescribers informally challenged the results, suggesting that this practice was driven by clinical need, not inherent bias. The validity of these views were tested by surveying the prescribing intention of doctors in a single trust, using a case vignette method. This built on earlier studies by exploring antipsychotic prescribing by ethnicity using a different research design. The study did not find differences in antipsychotic prescribing intention by ethnicity for dose, high dose, polypharmacy, type and route of administration outcomes were found although there were significant limitations.

Overall the clinical and theoretical studies in this thesis did not show differences in antipsychotic prescribing by ethnicity but there were significant limitations in study design and analysis.

6.2 Improvement of Studies in Thesis

Description of the evolution of the studies in this thesis are described in Chapters 2 and 5. Both were helped immeasurably by examining previous research work (see Appendices 2, 3 and 4), preliminary studies in this field (Appendices 6 and 9) and comments from peer-reviewers during the publication process.

The clinical studies were limited by several factors that may have produced the negative findings - their cross-sectional design, broad categorisation of ethnic groups, smaller numbers of some ethnic groups (i.e. Asian, mixed, Chinese/other), no assessment of severity of mental state (CGI-S was collected previously but not measured at the time of antipsychotic prescription so was not a useful measure), some missing data, possible overadjustment of outcomes with multiple variables in regression models and an

inpatient population only. Despite these there was a large total sample size, multiple centres, collection of a large number of confounding variables, missing data was accounted for statistically and data analysed in several ways.

Changes to the clinical studies that, with the benefit of hindsight, could have improved methodology include using more categories of ethnic group e.g. black African, black Caribbean, adding centres with low proportions of ethnic minority groups (to see effect of prescribing in a non-multicultural environment), powering the study so individual centre effects could be detected, using multilevel modelling for analysis of data by centre to measure cluster effects, collecting more confounding variables to improve the predictive power of regression models, extending the sample to include community patients, ensuring data collectors filled in the study forms properly, ensuring outcomes were not subject to the effects of overadjustment and using a different study design.

For the case vignette study in Chapter 5 greater efforts could have been made to improve the questionnaire response rate by changing the way they were distributed, increasing the numbers of prescribers surveyed and having a more rigorous follow-up process. Improved validity of the clinical and theoretical studies with these changes would have required more time and consequently greater research funds.

6.3 Contribution of Thesis to Field of Antipsychotic Prescribing and Ethnicity

Some of the studies in this thesis have contributed substantially to the field of antipsychotic prescribing and ethnicity. The study described in Chapter 2 was the largest UK multicentre study of antipsychotic prescribing in black and white patients at the time of data collection and publication (there has since been a larger study by Das-Munshi *et al*, 2018). The previous studies at the time did not include such a large sample and geographical spread and so the findings were therefore limited. Other UK studies of antipsychotics and ethnicity were also much smaller, older, single-centred and measured fewer prescribing outcomes and confounding variables than described in this thesis (Connolly et al., 2007; Lloyd & Moodley, 1992; Shubsachs et al., 1995; Stanley & Doyle, 1993; Tunnicliffe et al., 1992). The studies in Chapter 2 and 4 were published (see Appendices 14 and 15) in peer-reviewed journals and have been cited by other researchers in this field (Cook et al., 2015; Hassan et al., 2013; Takeshita et al., 2014; Thompson et al., 2016).

The case vignette study of theoretical choice of antipsychotic by ethnicity in Chapter 5 updated previous studies and took the premise further (Lewis et al., 1990; Minnis et al., 2001). Previous studies had only analysed 'antipsychotic use indicated' whilst this study examined several outcomes of antipsychotic prescribing. This study was also published (see Appendix 20).

The study was funded by the Equality and Human Rights Commission (formerly the Commission for Racial Equality at the time of study initiation). This was not via a grant

but a direct approach with a request to undertake the study as they recognised the importance of earlier work in this field and the value of a multicentre study of all ethnicities.

6.4 Recommendations

6.4.1 Recommendations for Clinical Practice

Overall antipsychotic prescribing was not affected by ethnicity in the studies described in this thesis but analysis of data by individual centre did reveal some differences. The significant limitations of the study may have resulted in negative findings. It is recommended that all providers of mental health services monitor antipsychotic prescribing by ethnicity and, if differences are found, investigate and remedy these discrepancies.

6.4.2 Recommendations for Prescribers

The UK studies described in this thesis found that antipsychotic prescribing does not vary by ethnicity for inpatients. It is recommended that prescribers reassure patients and carers that concerns about this issue have been recognised and investigated but that further studies are needed to overcome the limitations of research already undertaken.

Prescribers are encouraged and educated to avoid, where possible, the use of high doses and combinations of antipsychotics and, where feasible, use clozapine in treatment-resistant illness and long-acting injections where non-compliance is suspected.

6.4.3 Recommendations for Future Research

The research studies undertaken for this thesis were thorough and, within the limits of their inherent design flaws, well conducted. A different design could have resulted in a

more rigorous study, for example using a prospective cohort study. This would allow assessment of illness severity on initiation of an antipsychotic – a limitation of this study design. Also using different methods of assessing dose, for instance CPZe or defined daily doses, could be employed as were done in earlier studies (see Appendix 6), expanding the ethnic group categories to allow analysis of within not just between group differences and adjusting for fewer cofounding factors to avoid overadjustment. Completion of a meta-analysis of antipsychotic prescribing in ethnic minorities, incorporating the studies in Appendix 3, would be a robust method of analysing antipsychotic use by ethnicity. A meta-analysis has been performed before but only examined two outcomes (antipsychotic use and type) in a community sample (Puyat et al., 2013).

Extending the reach of the study to a greater number of centres and including community patients could be achieved by adding ethnicity and antipsychotic prescribing to the audit topics of POMH-UK. This is because most NHS mental health trusts, along with private facilities and charitable institutions, are members of this quality measurement and improvement body. This would also allow collection of data from centres where ethnic groups are in the minority, in comparison to these studies where patients were recruited from NHS trusts with the largest proportions of ethnic minority patients. In addition re-auditing the centres in this study would be advised, particularly those where differences by ethnicity have been found, to determine if changes to the culture and quality of prescribing have occurred.

REFERENCES

Acheson, D. (1998). *Independent Inquiry into Inequalities in Health Report*. Department of Health.

Ackenheil, M. and Weber, K. (2004). Differing response to antipsychotic therapy in schizophrenia: pharmacogenomic aspects. *Dialogues in clinical neuroscience* **6**(1): 71-77.

Adams, G. L., Dworkin, R. J. and Rosenberg, S. D. (1984). Diagnosis and pharmacotherapy issues in the care of Hispanics in the public sector. *American journal of psychiatry* **141**(8): 970-974.

Aggarwal, N. K., Rosenheck, R. A., Woods, S. W. and Sernyak, M. J. (2012a). Race and long-acting antipsychotic prescription at a community mental health center: a retrospective chart review. *Journal of clinical psychiatry* **73**(4): 513-517.

Aggarwal, N. K., Sernyak, M. J. and Rosenheck, R. A. (2012b). Prevalence of concomitant oral antipsychotic drug use among patients treated with long-acting, intramuscular, antipsychotic medications. *Journal of clinical psychopharmacology* **32**(3): 323-328.

Alegria, M., Chatterji, P., Wells, K., Cao, Z., Chen, C. N., Takeuchi, D., Jackson, J. and Meng, X. L. (2008). Disparity in depression treatment among racial and ethnic minority populations in the United States. *Psychiatric services* **59**(11): 1264-1272.

Allmark, P. (2004). Should research samples reflect the diversity of the population? *Journal of medical ethics* **30**(2): 185-189.

Arnold, J. G., Miller, A. L., Canive, J. M., Rosenheck, R. A., Swartz, M. S. and Mintz, J. (2013). Comparison of outcomes for African Americans, Hispanics, and Non-Hispanic Whites in the CATIE study. *Psychiatric services* **64**(6): 570-578.

Arnold, L. M., Strakowski, S. M., Schwiers, M. L., Amicone, J., Fleck, D. E., Corey, K. B. and Farrow, J. E. (2004). Sex, ethnicity, and antipsychotic medication use in patients with psychosis. *Schizophrenia research* **66**(2-3): 169-175.

Ascher-Svanum, H., Peng, X., Montgomery, W., Faries, D. E., Lawson, A. H., Witte, M. M., Novick, D., Jemiai, N., Perrin, E. and McDonnell, D. P. (2011). Assessing the infrequent oral supplementation of olanzapine long-acting injection in the treatment of schizophrenia. *European psychiatry* **26**(5): 313-319.

Aspinall, P. and Jacobson, B. (2004). *Ethnic disparities in health and health care: a focussed review of the evidence and selected examples of good practice* London, London Health Observatory.

Bagchi, A., Sambamoorthi, U., McSpiritt, E., Yanos, P., Walkup, J. and Crystal, S. (2004). Use of antipsychotic medications among HIV-infected individuals with schizophrenia. *Schizophrenia research* **71**(2-3): 435-444.

Baillargeon, J. and Contreras, S. A. (2001). Antipsychotic prescribing patterns in the Texas prison system. *Journal of the American Academy of Psychiatry and the Law* **29**(1): 48-53.

Ball, J. K. and Elixhauser, A. (1996). Treatment differences between blacks and whites with colorectal cancer. *Medical care* **34**(9): 970-984.

Barnard, L., Young, A. H., Pearson, J., Geddes, J. and O'Brien, G. (2002). A systematic review of the use of atypical antipsychotics in autism. *Journal of psychopharmacology* **16**(1): 93-101.

Barnes, A. (2004). Race, Schizophrenia, and Admission to State Psychiatric Hospitals. *Administration and policy in mental health and mental health services research* **31**(3): 241-252.
Barnes, A. (2008). Race and hospital diagnoses of schizophrenia and mood disorders. *Social work* **53**(1): 77-83.
Barnes, T. R. and Paton, C. (2011). Antipsychotic polypharmacy in schizophrenia: benefits and risks. *CNS drugs* **25**(5): 383-399.
Barnes, T. R., Shingleton-Smith, A. and Paton, C. (2009). Antipsychotic long-acting injections: prescribing practice in the UK. *British journal of psychiatry. Supplement* **52**: S37-42.
Bayard-Burfield, L., Sundquist, J. and Johansson, S. E. (2001). Ethnicity, self reported psychiatric illness, and intake of psychotropic drugs in five ethnic groups in Sweden. *Journal of epidemiology and community health* **55**(9): 657-664.
Becares, L. (2013). *Which ethnic groups have the poorest health? Ethnic health inequalities 1991 to 2011*. Manchester, Centre on Dynamics of Ethnicity. University of Manchester.
Benzeval, M., Judge, K, Whitehead, M. (1995). *Tackling Inequalities in Health; an Agenda for Action*. London, The King's Fund.
Bernard, S., Neville, K. A., Nguyen, A. T. and Flockhart, D. A. (2006). Interethnic differences in genetic polymorphisms of CYP2D6 in the U.S. population: clinical implications. *The oncologist* **11**(2): 126-135.
Bhugra, D. and Bhui, K. (2001). African–Caribbeans and schizophrenia: contributing factors. *Advances in psychiatric treatment* **7**(4): 283-291.
Bhugra, D., Leff, J., Mallett, R., Der, G., Corridan, B. and Rudge, S. (1997). Incidence and outcome of schizophrenia in whites, African-Caribbeans and Asians in London. *Psychological medicine* **27**(4): 791-798.
Bhui, K., Stansfeld, S., Hull, S., Priebe, S., Mole, F. and Feder, G. (2003). Ethnic variations in pathways to and use of specialist mental health services in the UK. Systematic review. *British journal of psychiatry* **182**: 105-116.
Binder, R. L. and Levy, R. (1981). Extrapyramidal reactions in Asians. *American jounal of psychiatry* **138**(9): 1243-1244.
Bjurlin, M. A., Zhao, L. C., Goble, S. M. and Hollowell, C. M. (2012). Race and insurance status are risk factors for orchiectomy due to testicular trauma. *Journal of urology* **187**(3): 931-935.
Black, D. (1980). *Inequalities in Health: Report of a Research Working Group* London, Department of Health and Social Security.
Black, D. W., Zanarini, M. C., Romine, A., Shaw, M., Allen, J. and Schulz, S. C. (2014). Comparison of low and moderate dosages of extended-release quetiapine in borderline personality disorder: a randomized, double-blind, placebo-controlled trial. *American jounal of psychiatry* **171**(11): 1174-1182.
Boggs, D. L., Kelly, D. L., Feldman, S., McMahon, R. P., Nelson, M. W., Yu, Y. and Conley, R. R. (2008). Quetiapine at high doses for the treatment of refractory schizophrenia. *Schizophrenia research* **101**(1-3): 347-348.
Brandon, D. T., Isaac, L. A. and LaVeist, T. A. (2005). The legacy of Tuskegee and trust in medical care: is Tuskegee responsible for race differences in mistrust of medical care? *Journal of the National Medical Association* **97**(7): 951-956.
Brandt, A. M. (1978). Racism and research: the case of the Tuskegee Syphilis Study. *The Hastings Center report* **8**(6): 21-29.

Braunstein, J. B., Sherber, N. S., Schulman, S. P., Ding, E. L. and Powe, N. R. (2008). Race, Medical Researcher Distrust, Perceived Harm, and Willingness to Participate in Cardiovascular Prevention Trials. *Medicine* **87**(1): 1-9.

Breslow, N. (1982). Design and analysis of case-control studies. *Annual review of public health* **3**: 29-54.

British Medical Association and Royal Pharmaceutical Society of Great Britain (2008). *British National Formulary 55th Edition*. London, BMJ Group and Royal Pharmaceutical Society Publishing.

British Medical Journal Group and Pharmaceutical Press (2014). *British National Formulary 68th Edition*. London, BMJ Group and Pharmaceutical Press.

British Psychological Society (2016). Achieving representation in psychology. A BPS response. *Psychologist* **29**: 246-255.

Brown, D. R. and Topcu, M. (2003). Willingness to participate in clinical treatment research among older African Americans and Whites. *The Gerontologist* **43(1)**: 62-72.

Brown, J. D., Barrett, A., Caffery, E., Hourihan, K. and Ireys, H. T. (2014). State and demographic variation in use of depot antipsychotics by Medicaid beneficiaries with schizophrenia. *Psychiatric services* **65**(1): 121-124.

Buchanan, R. W., Kreyenbuhl, J., Kelly, D. L., Noel, J. M., Boggs, D. L., Fischer, B. A., Himelhoch, S., Fang, B., Peterson, E., Aquino, P. R. and Keller, W. (2010). The 2009 schizophrenia PORT psychopharmacological treatment recommendations and summary statements. *Schizophrenia bulletin* **36**(1): 71-93.

Burgio, K. L., Williams, B. R., Dionne-Odom, J. N., Redden, D. T., Noh, H., Goode, P. S., Kvale, E., Bakitas, M. and Bailey, F. A. (2016). Racial Differences in Processes of Care at End of Life in VA Medical Centers: Planned Secondary Analysis of Data from the BEACON Trial. *Journal of palliative medicine* **19**(2): 157-163.

Busch, A. B., Huskamp, H. A., Neelon, B., Manning, T., Normand, S. L. and McGuire, T. G. (2009a). Longitudinal racial/ethnic disparities in antimanic medication use in bipolar-I disorder. *Medical care* **47**(12): 1217-1228.

Busch, A. B., Lehman, A. F., Goldman, H. and Frank, R. G. (2009b). Changes over time and disparities in schizophrenia treatment quality. *Medical care* **47**(2): 199-207.

Cañas, F., Alptekin, K., Azorin, J. M., Dubois, V., Emsley, R., García, A. G., Gorwood, P., Haddad, P. M., Naber, D. and Olivares, J. M. (2013). Improving treatment adherence in your patients with schizophrenia. *Clinical drug investigation* **33**(2): 97-107.

Cantor-Graae, E., Pedersen, C. B., McNeil, T. F. and Mortensen, P. B. (2003). Migration as a risk factor for schizophrenia: a Danish population-based cohort study. *British journal of psychiatry* **182**.

Cantor-Graae, E. and Selten, J.-P. (2005). Schizophrenia and migration: a meta-analysis and review. *American journal of psychiatry*.

Cantwell, R., Brewin, J., Glazebrook, C., Dalkin, T., Fox, R., Medley, I. and Harrison, G. (1999). Prevalence of substance misuse in first-episode psychosis. *British journal of psychiatry* **174**: 150-153.

Care Quality Commission (2009). *Count me in 2009: Results of the 2009 national census of inpatients in mental health and learning disability services in England and Wales*. London.

Care Quality Commission (2010). *Count me in 2010: Results of the 2010 national census of inpatients in mental health and learning disability services in England and Wales*. London.

Carnahan, R. M., Lund, B. C., Perry, P. J. and Chrischilles, E. A. (2006). Increased risk of extrapyramidal side-effect treatment associated with atypical antipsychotic polytherapy. *Acta psychiatrica Scandinavica* **113**(2): 135-141.

Cataife, G. and Weinberg, D. A. (2015). Racial and Ethnic Differences in Antipsychotic Medication Use Among Children Enrolled in Medicaid. *Psychiatric services* **66**(9): 946-951.

Centers for Disease Control and Prevention (1997). *U.S. Public Health Service Syphilis Study at Tuskegee, Presidential Apology*, Press Release.

Chakos, M. H., Glick, I. D., Miller, A. L., Hamner, M. B., Miller, D. D., Patel, J. K., Tapp, A., Keefe, R. S. and Rosenheck, R. A. (2006). Baseline use of concomitant psychotropic medications to treat schizophrenia in the CATIE trial. *Psychiatric services* **57**(8): 1094-1101.

Chen, E. Y., Harrison, G. and Standen, P. J. (1991). Management of first episode psychotic illness in Afro-Caribbean patients. *British journal of psychiatry* **158**: 517-522.

Chiu, M., Lebenbaum, M., Newman, A. M., Zaheer, J. and Kurdyak, P. (2016). Ethnic Differences in Mental Illness Severity: A Population-Based Study of Chinese and South Asian Patients in Ontario, Canada. *Journal of clinical psychiatry*.

Chung, H., Mahler, J. C. and Kakuma, T. (1995). Racial differences in treatment of psychiatric inpatients. *Psychiatric services* **46**(6): 586-591.

Ciliberto, N., Bossie, C. A., Urioste, R. and Lasser, R. A. (2005). Lack of impact of race on the efficacy and safety of long-acting risperidone versus placebo in patients with schizophrenia or schizoaffective disorder. *International clinical psychopharmacology* **20**(4): 207-212.

Clark, T. and Rowe, R. (2006). Violence, stigma and psychiatric diagosis: the effects of a history of violence on psychiatric diagnosis. *Psychiatric bulletin* **30**: 254-256.

Collazo, Y., Tam, R., Sramek, J. and Herrera, J. (1996). Neuroleptic dosing in Hispanic and Asian Inpatients with schizophrenia. *The Mount Sinai journal of medicine* **63**(5-6): 310-313.

Commander, M. J., Dharan, S. P., Odell, S. M. and Surtees, P. G. (1997). Access to mental health care in an inner-city health district. II: Association with demographic factors. *British journal of psychiatry* **170**: 317-320.

Connolly, A., Rogers, P. and Taylor, D. (2007). Antipsychotic prescribing quality and ethnicity: a study of hospitalized patients in south east London. *Journal of psychopharmacology* **21**(2): 191-197.

Connolly, A. and Taylor, D. (2008). Ethnicity and quality of antipsychotic prescribing among in-patients in south London. *British journal of psychiatry* **193**(2): 161-162.

Connolly, A., Taylor, D., Sparshatt, A. and Cornelius, V. (2011). Antipsychotic prescribing in Black and White hospitalised patients. *Journal of psychopharmacology* **25**(5): 704-709.

Constantine, R. J., Andel, R. and Tandon, R. (2010a). Trends in adult antipsychotic polypharmacy: progress and challenges in Florida's Medicaid program. *Community mental health journal* **46**(6): 523-530.

Constantine, R. J., Boaz, T. and Tandon, R. (2010b). Antipsychotic polypharmacy in the treatment of children and adolescents in the fee-for-service component of a large state Medicaid program. *Clinical therapeutics* **32**(5): 949-959.

Cook, B. L., Carson, N. J., Kafali, E. N., Valentine, A., Rueda, J. D., Coe-Odess, S. and Busch, S. (2017). Examining psychotropic medication use among youth in the U.S. by race/ethnicity and psychological impairment. *General hospital psychiatry* **45**: 32-39.

Cook, T. B., Reeves, G. M., Teufel, J. and Postolache, T. T. (2015). Persistence of racial disparities in prescription of first-generation antipsychotics in the USA. *Pharmacoepidemiology and drug safety* **24**(11): 1197-1206.

Cooper, L. A., Gonzales, J. J., Gallo, J. J., Rost, K. M., Meredith, L. S., Rubenstein, L. V., Wang, N. Y. and Ford, D. E. (2003). The acceptability of treatment for depression among African-American, Hispanic, and white primary care patients. *Medical care* **41**(4): 479-489.

Copeland, L. A., Zeber, J. E., Valenstein, M. and Blow, F. C. (2003). Racial disparity in the use of atypical antipsychotic medications among veterans. *American journal of psychiatry* **160**(10): 1817-1822.

Corbie-Smith, G. (1999). The continuing legacy of the Tuskegee Syphilis Study: considerations for clinical investigation. *American journal of the medical sciences* **317**(1): 5-8.

Corbie-Smith, G., Thomas, S. B. and St George, D. M. (2002). Distrust, race, and research. *Archives of internal medicine* **162**(21): 2458-2463.

Cornwell, J. and Hull, S. (1998). Do GPs prescribe antidepressants differently for South Asian patients? *Family practice* **15**: S16-18.

Correll, C. U., Frederickson, A. M., Kane, J. M. and Manu, P. (2007). Does antipsychotic polypharmacy increase the risk for metabolic syndrome? *Schizophrenia research* **89**(1-3): 91-100.

Coury, D. L., Anagnostou, E., Manning-Courtney, P., Reynolds, A., Cole, L., McCoy, R., Whitaker, A. and Perrin, J. M. (2012). Use of psychotropic medication in children and adolescents with autism spectrum disorders. *Pediatrics* **130 Suppl 2**: S69-76.

Covell, N. H., Jackson, C. T., Evans, A. C. and Essock, S. M. (2002). Antipsychotic prescribing practices in Connecticut's public mental health system: rates of changing medications and prescribing styles. *Schizophrenia bulletin* **28**(1): 17-29.

Crombie, I., Irvine, L, Eiliott, L, Wallace, W. (2005). *Closing the Health Inequalities Gap: An International Perspective*, World Health Organization.

Cruz, I., Serna, C., Rue, M., Real, J., Galvan, L. and Pifarre, J. (2012). Comparative exposure to antipsychotic medications in immigrant and native-born populations of a Spanish health region. *European psychiatry* **27**(7): 477-482.

Das-Munshi, J., Bhugra, D. and Crawford, M. J. (2018). Ethnic minority inequalities in access to treatments for schizophrenia and schizoaffective disorders: findings from a nationally representative cross-sectional study. *BMC Med* **16**(1): 55.

Datapharm Communications Ltd. (2016). "*Electronic Medicines Compendium*." Available at: http://www.medicines.org.uk/emc/ (Accessed: 1st November 2016).

Daumit, G. L., Crum, R. M., Guallar, E., Powe, N. R., Primm, A. B., Steinwachs, D. M. and Ford, D. E. (2003). Outpatient prescriptions for atypical antipsychotics for African Americans, Hispanics, and whites in the United States. *Archives of general psychiatry* **60**(2): 121-128.

Davies, S., Thornicroft, G., Leese, M., Higgingbotham, A. and Phelan, M. (1996). Ethnic differences in risk of compulsory psychiatric admission among

representative cases of psychosis in London. *British medical journal* **312**(7030): 533-537.
Davis, J. M. and Chen, N. (2004). Dose response and dose equivalence of antipsychotics. *Journal of clinical psychopharmacology* **24**(2): 192-208.
Degenhardt, E. K., Tamayo, J. M., Jamal, H. H., Gatz, J., Tohen, M. and Durell, T. M. (2011). Relationship between African-American or Caucasian origin and outcomes in the olanzapine treatment of acute mania: a pooled analysis of three adult studies conducted in the United States of America. *International clinical psychopharmacology* **26**(3): 141-145.
Delbello, M. P., Soutullo, C. A. and Strakowski, S. M. (2000). Racial differences in treatment of adolescents with bipolar disorder. *The American journal of psychiatry* **157**(5): 837-838.
Department of Health (1999a). *National Service Framework for Mental Health*. London.
Department of Health (1999b). *Saving lives: our healthier nation*. London.
Department of Health (2001). *A practical guide to ethnic monitoring in the NHS and social care*. London.
Department of Health (2003). *Inside Outside: Improving mental health services for black and minority ethnic communities in England.* London.
Department of Health (2005a). *Delivering race equality in mental health care: an action plan for reform inside and outside services and the Government's response to the independent inquiry into the death of David Bennett*. London.
Department of Health (2005b). *Research governance framework for health and social care 2nd edition*, London.
Department of Health (2007). *A practical guide to ethnic monitoring in the NHS and social care*. London.
Department of Health (2009). *Improving Access to Psychological Therapies (IAPT). Black and Minority Ethnic (BME) Positive Practice Guide*. London.
Department of Health (2011). *No health without mental health*. London.
Depp, C., Ojeda, V. D., Mastin, W., Unutzer, J. and Gilmer, T. P. (2008). Trends in use of antipsychotics and mood stabilizers among Medicaid beneficiaries with bipolar disorder, 2001-2004. *Psychiatric services* **59**(10): 1169-1174.
Dey, S., Menkes, D. B., Obertova, Z., Chaudhuri, S. and Mellsop, G. (2016). Antipsychotic prescribing and its correlates in New Zealand. *Australasian psychiatry* **24**(4): 360-364.
Di Forti, M., Marconi, A., Carra, E., Fraietta, S., Trotta, A., Bonomo, M., Bianconi, F., Gardner-Sood, P., O'Connor, J., Russo, M., Stilo, S. A., Marques, T. R., Mondelli, V., Dazzan, P., Pariante, C., David, A. S., Gaughran, F., Atakan, Z., Iyegbe, C., Powell, J., Morgan, C., Lynskey, M. and Murray, R. M. (2015). Proportion of patients in south London with first-episode psychosis attributable to use of high potency cannabis: a case-control study. *The lancet. Psychiatry* **2**(3): 233-238.
Diaz, F. J. and De Leon, J. (2002). Excessive antipsychotic dosing in 2 U.S. State hospitals. *Journal of clinical psychiatry* **63**(11): 998-1003.
Dickey, B., Normand, S. L., Eisen, S., Hermann, R., Cleary, P., Cortes, D. and Ware, N. (2006). Associations between adherence to guidelines for antipsychotic dose and health status, side effects, and patient care experiences. *Medical care* **44**(9): 827-834.
Domino, M. E. and Swartz, M. S. (2008). Who are the new users of antipsychotic medications? *Psychiatric services* **59**(5): 507-514.

dosReis, S., Zito, J. M., Buchanan, R. W. and Lehman, A. F. (2002). Antipsychotic dosing and concurrent psychotropic treatments for Medicaid-insured individuals with schizophrenia. *Schizophrenia bulletin* **28**(4): 607-617.

Douzenis, A., Apostolopoulos, A., Seretis, D., Rizos, E. N., Christodoulou, C. and Lykouras, L. (2011). The effect of ethnicity on prescribing practice and treatment outcome in inpatients suffering from schizophrenia in Greece. *BMC psychiatry* **11**: 66.

Dunn, J. and Fahy, T. A. (1990). Police admissions to a psychiatric hospital. Demographic and clinical differences between ethnic groups. *British journal of psychiatry* **156**: 373-378.

Dusetzina, S. B., Cook, B. L., Busch, A. B., Alexander, G. C. and Huskamp, H. A. (2013). Racial-ethnic differences in incident olanzapine use after an FDA advisory for patients with schizophrenia. *Psychiatric services* **64**(1): 83-87.

el-Badri, S. and Mellsop, G. (2011). Clozapine use and outcomes among patients with treatment resistant schizophrenia. *Australasian psychiatry* **19**(5): 410-414.

el-Sadr, W. and Capps, L. (1992). The challenge of minority recruitment in clinical trials for AIDS. *Journal of the American Medical Association* **267**(7): 954-957.

Elie, D., Poirier, M., Chianetta, J., Durand, M., Gregoire, C. and Grignon, S. (2010). Cognitive effects of antipsychotic dosage and polypharmacy: a study with the BACS in patients with schizophrenia and schizoaffective disorder. *Journal of psychopharmacology* **24**(7): 1037-1044.

Emsley, R. A., Roberts, M. C., Rataemane, S., Pretorius, J., Oosthuizen, P. P., Turner, J., Niehaus, D. J., Keyter, N. and Stein, D. J. (2002). Ethnicity and treatment response in schizophrenia: a comparison of 3 ethnic groups. *Journal of clinical psychiatry* **63**(1): 9-14.

Ezewuzie, N. and Taylor, D. (2006). Establishing a dose-response relationship for oral risperidone in relapsed schizophrenia. *Journal of psychopharmacology* **20**(1): 86-90.

Fastenau, J., Campbell, R. S., Nathanson, B. H., Haidar, T., Yi, J. and Wade, R. (2012). Factors Associated with Real-World Inpatient Use of Long-Acting Atypical Antipsychotics. *Value in health* **15**(4): A84.

Fearon, P. and Murray, R. (2007). "*Rapid response: Count Me In Census provides no compelling evidence of Institutional Racism (letter)*." Available at: http://www.bmj.com/rapid-response/2011/11/01/count-me-census-provides-no-compelling-evidence-institutional-racism (Accessed: 20th January 2016).

Feder, G., Crook, A. M., Magee, P., Banerjee, S., Timmis, A. D. and Hemingway, H. (2002). Ethnic differences in invasive management of coronary disease: prospective cohort study of patients undergoing angiography. *British medical journal* **324**(7336): 511-516.

Federal Drugs Administration (2013). Collection, Analysis, and Availability of Demographic Subgroup Data for FDA-Approved Medical Products

Feinglass, J., Rucker-Whitaker, C., Lindquist, L., McCarthy, W. J. and Pearce, W. H. (2005). Racial differences in primary and repeat lower extremity amputation: results from a multihospital study. *Journal of vascular surgery* **41**(5): 823-829.

Fenton, W. S., Blyler, C. R. and Heinssen, R. K. (1997). Determinants of medication compliance in schizophrenia: empirical and clinical findings. *Schizophrenia bulletin* **23**(4): 637-651.

Ferguson, D. G., Glesener, D. C. and Raschick, M. (2006). Psychotropic drug use with European American and American Indian children in foster care. *Journal of child and adolescent psychopharmacology* **16**(4): 474-481.

Field, A. (2013). *Discovering Statistics using IBM SPSS Statistics*. 4th Ed. London, SAGE Publications Ltd.

Findling, R. L., Horwitz, S. M., Birmaher, B., Kowatch, R. A., Fristad, M. A., Youngstrom, E. A., Frazier, T. W., Axelson, D., Ryan, N., Demeter, C. A., Depew, J., Fields, B., Gill, M. K., Deyling, E. A., Rowles, B. M. and Arnold, L. E. (2011). Clinical characteristics of children receiving antipsychotic medication. *Journal of child and adolescent psychopharmacology* **21**(4): 311-319.

Fisher, J. A. and Kalbaugh, C. A. (2011). Challenging assumptions about minority participation in US clinical research. *American journal of public health* **101**(12): 2217-2222.

Flaskerud, J. H. and Hu, L. T. (1992). Racial/ethnic identity and amount and type of psychiatric treatment. *American jounal of psychiatry* **149**(3): 379-384.

Flaskerud, J. H. and Liu, P. Y. (1991). Effects of an Asian client-therapist language, ethnicity and gender match on utilization and outcome of therapy. *Community mental health journal* **27**(1): 31-42.

Fleck, D. E., Hendricks, W. L., DelBello, M. P. and Strakowski, S. M. (2002). Differential prescription of maintenance antipsychotics to African American and white patients with new-onset bipolar disorder. *Journal of clinical psychiatry* **63**(8): 658-664.

Fleischhacker, W. W., Heikkinen, M. E., Olie, J. P., Landsberg, W., Dewaele, P., McQuade, R. D., Loze, J. Y., Hennicken, D. and Kerselaers, W. (2010). Effects of adjunctive treatment with aripiprazole on body weight and clinical efficacy in schizophrenia patients treated with clozapine: a randomized, double-blind, placebo-controlled trial. *International journal of neuropsychopharmacology* **13**(8): 1115-1125.

Frackiewicz, E. J., Herrera, J. M., Sramek, J. J., Collazo, Y. and Lawson, W. B. (2002). Risperidone in the treatment of Hispanic inpatients with schizophrenia: a pilot study. *Psychiatry* **65**(4): 371-374.

Gamble, V. N. (1997). Under the shadow of Tuskegee: African Americans and health care. *American journal of public health* **87**(11): 1773-1778.

Gardner, D. M., Murphy, A. L., O'Donnell, H., Centorrino, F. and Baldessarini, R. J. (2010). International consensus study of antipsychotic dosing. *American journal of psychiatry* **167**(6): 686-693.

Garver, D., Lazarus, A., Rajagopalan, K., Lamerato, L., Katz, L. M., Stern, L. S., Dolgitser, M. and Doyle, J. J. (2006). Racial differences in medication switching and concomitant prescriptions in the treatment of bipolar disorder. *Psychiatric services* **57**(5): 666-672.

Gary, F. A. (2005). Stigma: barrier to mental health care among ethnic minorities. *Issues in mental health nursing* **26**(10): 979-999.

Geddes, J., Mercer, G., Frith, C. D., MacMillan, F., Owens, D. G. and Johnstone, E. C. (1994). Prediction of outcome following a first episode of schizophrenia. A follow-up study of Northwick Park first episode study subjects. *British journal of psychiatry* **165**(5): 664-668.

Gee, S., Vergunst, F., Howes, O. and Taylor, D. (2014). Practitioner attitudes to clozapine initiation. *Acta psychiatrica Scandinavica* **130**(1): 16-24.

Gee, S. H., Shergill, S. S. and Taylor, D. M. (2016). Factors associated with changes in hospitalisation in patients prescribed clozapine. *Journal of psychopharmacology* **30**(8): 819-825.

Gersing, K., Burchett, B., March, J., Ostbye, T. and Krishnan, K. R. (2007). Predicting antipsychotic use in children. *Psychopharmacology bulletin* **40**(3): 116-124.
Givens, J. L., Houston, T. K., Van Voorhees, B. W., Ford, D. E. and Cooper, L. A. (2007a). Ethnicity and preferences for depression treatment. *General hospital psychiatry* **29**(3): 182-191.
Givens, J. L., Katz, I. R., Bellamy, S. and Holmes, W. C. (2007b). Stigma and the acceptability of depression treatments among African Americans and whites. *Journal of general internal medicine* **22**(9): 1292-1297.
Glazer, W. M., Morgenstern, H. and Doucette, J. (1994). Race and tardive dyskinesia among outpatients at a CMHC. *Hospital & community psychiatry* **45**(1): 38-42.
Glover, G., Webb, M. and Evison, F. (2010). *Improving access to psychological therapies - year one sites data review*. Durham, North East Health Observatory.
Goel, M. S., Wee, C. C., McCarthy, E. P., Davis, R. B., Ngo-Metzger, Q. and Phillips, R. S. (2003). Racial and ethnic disparities in cancer screening: the importance of foreign birth as a barrier to care. *Journal of general internal medicine* **18**(12): 1028-1035.
Goldacre, M. J., Davidson, J. M. and Lambert, T. W. (2004). Country of training and ethnic origin of UK doctors: database and survey studies. *British medical journal* **329**(7466): 597.
Gomez, S. L. and Glaser, S. L. (2006). Misclassification of race/ethnicity in a population-based cancer registry (United States). *Cancer causes & control* **17**(6): 771-781.
Gonzalez, H. M., Croghan, T., West, B., Williams, D., Nesse, R., Tarraf, W., Taylor, R., Hinton, L., Neighbors, H. and Jackson, J. (2008). Antidepressant use in black and white populations in the United States. *Psychiatric services* **59**(10): 1131-1138.
Gray, R., Headley, J. and Oakley, L. (2009). *Inequalities in Infant Mortality Project Briefing Paper 3. Towards an understanding of variations in infant mortality rates between different ethnic groups in England and Wales*. Oxford, National Perinatal Epidemiology Unit, University of Oxford.
Grech, P. and Taylor, D. (2012). Long-term antipsychotic polypharmacy: how does it start, why does it continue? *Therapeutic advances in psychopharmacology* **2**(1): 5-11.
Green, S. B. (1991). How Many Subjects Does It Take To Do A Regression Analysis. *Multivariate behavioral research* **26**(3): 499-510.
Grossman, I., Sullivan, P. F., Walley, N., Liu, Y., Dawson, J. R., Gumbs, C., Gaedigk, A., Leeder, J. S., McEvoy, J. P., Weale, M. E. and Goldstein, D. B. (2008). Genetic determinants of variable metabolism have little impact on the clinical use of leading antipsychotics in the CATIE study. *Genetics in medicine* **10**(10): 720-729.
Haddad, P. (2005). Weight change with atypical antipsychotics in the treatment of schizophrenia. *Journal of psychopharmacology* **19**(6 suppl): 16-27.
Haddad, P. and Wieck, A. (2004). Antipsychotic-induced hyperprolactinaemia. *Drugs* **64**(20): 2291-2314.
Hanlon, J. T., Wang, X., Good, C. B., Rossi, M. I., Stone, R. A., Selma, T. P. and Handler, S. M. (2009). Racial differences in medication use among older, long-stay Veterans Affairs nursing home care unit patients. *Consultant pharmacist* **24**(6): 439-446.

Harrington, M., Lelliott, P., Paton, C., Okocha, C., Duffett, R. and Sensky, T. (2002). The results of a multi-centre audit of the prescribing of antipsychotic drugs for in-patients in the UK. *Psychiatrist* **26**(11): 414-418.

Hashmi, A., Rahim, A. and Sharif, M. S. (2009). Antipsychotic prescription trends according to ethnicity. *Psychiatrist* **33**(8): 313-314.

Hassan, A., Teo, C., Kennedy, J. L., Ravindran, A. and De Luca, V. (2013). Association of ethnicity with antipsychotic dosage using STRUCTURE analysis. *Pharmacopsychiatry* **46**(4): 151-155.

Health and Social Care Information Centre (2015). *Mental Health Bulletin Annual Statistics 2014-2015*.

Health Research Authority. (2014). "*Is my study research?*" Available at: http://www.hra-decisiontools.org.uk/research/ (Accessed: 10th January 2014).

Henderson, D. C., Fan, X., Copeland, P. M., Sharma, B., Borba, C. P., Boxill, R., Freudenreich, O., Cather, C., Evins, A. E. and Goff, D. C. (2009). Aripiprazole added to overweight and obese olanzapine-treated schizophrenia patients. *Journal of clinical psychopharmacology* **29**(2): 165-169.

Herbeck, D. M., West, J. C., Ruditis, I., Duffy, F. F., Fitek, D. J., Bell, C. C. and Snowden, L. R. (2004). Variations in use of second-generation antipsychotic medication by race among adult psychiatric patients. *Psychiatric services* **55**(6): 677-684.

Herzig, S. J., Rothberg, M. B., Guess, J. R., Stevens, J. P., Marshall, J., Gurwitz, J. H. and Marcantonio, E. R. (2016). Antipsychotic Use in Hospitalized Adults: Rates, Indications, and Predictors. *Journal of the American Geriatrics Society* **64**(2): 299-305.

Hickling, F. W., McKenzie, K., Mullen, R. and Murray, R. (1999). A Jamaican psychiatrist evaluates diagnoses at a London psychiatric hospital. *British journal of psychiatry* **175**: 283-285.

Hodgins, S. and Riaz, M. (2011). Violence and phases of illness: differential risk and predictors. *European psychiatry* **26**(8): 518-524.

Holden, T. J. (1987). Tardive dyskinesia in long-term hospitalised Zulu psychiatric patients. A prevalence study. *South African medical journal* **71**(2): 88-90.

Honer, W. G., MacEwan, G. W., Gendron, A., Stip, E., Labelle, A., Williams, R. and Eriksson, H. (2012). A randomized, double-blind, placebo-controlled study of the safety and tolerability of high-dose quetiapine in patients with persistent symptoms of schizophrenia or schizoaffective disorder. *Journal of clinical psychiatry* **73**(1): 13-20.

Horvitz-Lennon, M., Alegria, M. and Normand, S. L. (2012). The effect of race-ethnicity and geography on adoption of innovations in the treatment of schizophrenia. *Psychiatric services* **63**(12): 1171-1177.

Horvitz-Lennon, M., Donohue, J. M., Lave, J. R., Alegria, M. and Normand, S. L. (2013). The effect of race-ethnicity on the comparative effectiveness of clozapine among Medicaid beneficiaries. *Psychiatric services* **64**(3): 230-237.

Hosmer, D. and Lemeshow, S. (2000). *Applied Logistic Regression*. United States of America: Wiley Blackwell.

Howes, O. D., Vergunst, F., Gee, S., McGuire, P., Kapur, S. and Taylor, D. (2012). Adherence to treatment guidelines in clinical practice: study of antipsychotic treatment prior to clozapine initiation. *British journal of psychiatry* **201**(6): 481-485.

Hsieh, K.-P., Lin, Y.-Y., Cheng, C.-L., Lai, M.-L., Lin, M.-S., Siest, J.-P. and Huang, J.-D. (2001). Novel mutations of CYP3A4 in Chinese. *Drug metabolism and disposition* **29**(3): 268-273.

Hudson, T. J., Cody, M., Armitage, T. L., Curtis, M. A. and Sullivan, G. (2005). Disparities in use of antipsychotic medications among nursing home residents in Arkansas. *Psychiatric services* **56**(6): 749-751.

Hutchinson, G., Takei, N., Fahy, T. A., Bhugra, D., Gilvarry, C., Moran, P., Mallett, R., Sham, P., Leff, J. and Murray, R. M. (1996). Morbid risk of schizophrenia in first-degree relatives of white and African-Caribbean patients with psychosis. *British journal of psychiatry* **169**(6): 776-780.

Jablensky, A., Sartorius, N., Ernberg, G., Anker, M., Korten, A., Cooper, J., Day, R. and Bertelsen, A. (1992). Schizophrenia: manifestations, incidence and course in different cultures A World Health Organization Ten-Country Study. *Psychological medicine. Monograph supplement* **20**: 1-97.

Jaffe, A. B. and Levine, J. (2003). Antipsychotic medication coprescribing in a large state hospital system. *Pharmacoepidemiology and drug safety* **12**(1): 41-48.

Jann, M. W., Chang, W. H., Lam, Y. W., Hwu, H. G., Lin, H. N., Chen, H., Chen, T. Y., Lin, S. K., Chien, C. P., Davis, C. M. and et al. (1992). Comparison of haloperidol and reduced haloperidol plasma levels in four different ethnic populations. *Progress in neuro-psychopharmacology & biological psychiatry* **16**(2): 193-202.

Jano, E., Johnson, M., Chen, H. and Aparasu, R. R. (2008). Determinants of atypical antipsychotic use among antipsychotic users in community-dwelling elderly, 1996-2004. *Current medical research and opinion* **24**(3): 709-716.

Janssen, I., Hanssen, M., Bak, M., Bijl, R. V., de Graaf, R., Vollebergh, W., McKenzie, K. and van Os, J. (2003). Discrimination and delusional ideation. *British journal of psychiatry* **182**: 71-76.

Jeste, D. V., Lindamer, L. A., Evans, J. and Lacro, J. P. (1996). Relationship of ethnicity and gender to schizophrenia and pharmacology of neuroleptics. *Psychopharmacology bulletin* **32**(2): 243-251.

Jin, Y., Pollock, B. G., Coley, K., Miller, D., Marder, S. R., Florian, J., Schneider, L., Lieberman, J., Kirshner, M. and Bies, R. R. (2010). Population pharmacokinetics of perphenazine in schizophrenia patients from CATIE: impact of race and smoking. *Journal of clinical pharmacology* **50**(1): 73-80.

Johns, L. C., Nazroo, J. Y., Bebbington, P. and Kuipers, E. (2002). Occurrence of hallucinatory experiences in a community sample and ethnic variations. *British journal of psychiatry* **180**: 174-178.

Johnston, S. C., Fung, L. H., Gillum, L. A., Smith, W. S., Brass, L. M., Lichtman, J. H. and Brown, A. N. (2001). Utilization of intravenous tissue-type plasminogen activator for ischemic stroke at academic medical centers: the influence of ethnicity. *Stroke; a journal of cerebral circulation* **32**(5): 1061-1068.

Jones, S. R., Carley, S. and Harrison, M. (2003). An introduction to power and sample size estimation. *Emergency medicine journal* **20**(5): 453-458.

Joukamaa, M., Heliovaara, M., Knekt, P., Aromaa, A., Raitasalo, R. and Lehtinen, V. (2006). Schizophrenia, neuroleptic medication and mortality. *British journal of psychiatry* **188**: 122-127.

Kales, H. C., Neighbors, H. W., Blow, F. C., Taylor, K. K., Gillon, L., Welsh, D. E., Maixner, S. M. and Mellow, A. M. (2005). Race, gender, and psychiatrists' diagnosis and treatment of major depression among elderly patients. *Psychiatric services* **56**(6): 721-728.

Kamble, P., Chen, H., Johnson, M. L., Bhatara, V. and Aparasu, R. R. (2015). Concurrent use of stimulants and second-generation antipsychotics among children with ADHD enrolled in Medicaid. *Psychiatric services* **66**(4): 404-410.
Kane, J., Honigfeld, G., Singer, J. and Meltzer, H. (1988). Clozapine for the treatment-resistant schizophrenic. A double-blind comparison with chlorpromazine. *Archives of general psychiatry* **45**(9): 789-796.
Kapur, S. and Seeman, P. (2001). Does fast dissociation from the dopamine D(2) receptor explain the action of atypical antipsychotics?: A new hypothesis. *American journal of psychiatry* **158**(3): 360-369.
Kapur, S., Zipursky, R., Jones, C., Remington, G. and Houle, S. (2000). Relationship between dopamine D(2) occupancy, clinical response, and side effects: a double-blind PET study of first-episode schizophrenia. *American journal of psychiatry* **157**(4): 514-520.
Karlsen, S., Nazroo, J. Y., McKenzie, K., Bhui, K. and Weich, S. (2005). Racism, psychosis and common mental disorder among ethnic minority groups in England. *Psychological medicine* **35**(12): 1795-1803.
Katz, R. V., Green, B. L., Kressin, N. R., James, S. A., Wang, M. Q., Claudio, C. and Russell, S. L. (2009). Exploring the "legacy" of the Tuskegee Syphilis Study: a follow-up study from the Tuskegee Legacy Project. *Journal of the National Medical Association* **101**(2): 179-183.
Katz, R. V., Kegeles, S. S., Kressin, N. R., Green, B. L., James, S. A., Wang, M. Q., Russell, S. L. and Claudio, C. (2008). Awareness of the Tuskegee Syphilis Study and the US presidential apology and their influence on minority participation in biomedical research. *American journal of public health* **98**(6): 1137-1142.
Keating, F., Robertson, D., McCulloch, A. and Francis, E. (2002). *'Breaking the Circles of Fear' – a review of the relationship between mental health services and African and Caribbean communities*. London, The Sainsbury Centre for Mental Health.
Kelly, D. L., Dixon, L. B., Kreyenbuhl, J. A., Medoff, D., Lehman, A. F., Love, R. C., Brown, C. H. and Conley, R. R. (2006). Clozapine utilization and outcomes by race in a public mental health system: 1994-2000. *Journal of clinical psychiatry* **67**(9): 1404-1411.
Kelly, D. L., Kreyenbuhl, J., Dixon, L., Love, R. C., Medoff, D. and Conley, R. R. (2007). Clozapine underutilization and discontinuation in African Americans due to leucopenia. *Schizophrenia bulletin* **33**(5): 1221-1224.
Kilbourne, A. M. and Pincus, H. A. (2006). Patterns of psychotropic medication use by race among veterans with bipolar disorder. *Psychiatric services* **57**(1): 123-126.
Kim, H., Lim, S. W., Kim, S., Kim, J. W., Chang, Y. H., Carroll, B. J. and Kim, D. K. (2006). Monoamine transporter gene polymorphisms and antidepressant response in koreans with late-life depression. *Journal of the American Medical Association* **296**(13): 1609-1618.
Kim, J. E., Saw, A., Zane, N. W. and Murphy, B. L. (2014). Patterns of Utilization and Outcomes of Inpatient Psychiatric Treatment in Asian Americans. *Asian American journal of psychology* **5**(1): 35-43.
King, M., Coker, E., Leavey, G., Hoare, A. and Johnson-Sabine, E. (1994). Incidence of psychotic illness in London: comparison of ethnic groups. *British medical journal* **309**(6962): 1115-1119.
King, M., Nazroo, J., Weich, S., McKenzie, K., Bhui, K., Karlsen, S., Stansfeld, S., Tyrer, P., Blanchard, M., Lloyd, K., McManus, S., Sproston, K. and Erens, B.

(2005). Psychotic symptoms in the general population of England--a comparison of ethnic groups (The EMPIRIC study). *Social psychiatry and psychiatric epidemiology* **40**(5): 375-381.

Kirkbride, J. B., Fearon, P., Morgan, C., Dazzan, P., Morgan, K., Tarrant, J., Lloyd, T., Holloway, J., Hutchinson, G., Leff, J. P., Mallett, R. M., Harrison, G. L., Murray, R. M. and Jones, P. B. (2006). Heterogeneity in incidence rates of schizophrenia and other psychotic syndromes: findings from the 3-center AeSOP study. *Archives of general psychiatry* **63**(3): 250-258.

Koffman, J., Fulop, N. J., Pashley, D. and Coleman, K. (1997). Ethnicity and use of acute psychiatric beds: one-day survey in north and south Thames regions. *British journal of psychiatry* **171**: 238-241.

Koranek, A. M., Smith, T. L., Mican, L. M. and Rascati, K. L. (2012). Impact of the CATIE trial on antipsychotic prescribing patterns at a state psychiatric facility. *Schizophrenia research* **137**(1-3): 137-140.

Kreyenbuhl, J., Marcus, S. C., West, J. C., Wilk, J. and Olfson, M. (2007a). Adding or switching antipsychotic medications in treatment-refractory schizophrenia. *Psychiatric services* **58**(7): 983-990.

Kreyenbuhl, J., Valenstein, M., McCarthy, J. F., Ganoczy, D. and Blow, F. C. (2007b). Long-term antipsychotic polypharmacy in the VA health system: patient characteristics and treatment patterns. *Psychiatric services* **58**(4): 489-495.

Kreyenbuhl, J., Zito, J. M., Buchanan, R. W., Soeken, K. L. and Lehman, A. F. (2003). Racial disparity in the pharmacological management of schizophrenia. *Schizophrenia bulletin* **29**(2): 183-193.

Kuno, E. and Rothbard, A. B. (2002). Racial disparities in antipsychotic prescription patterns for patients with schizophrenia. *American journal of psychiatry* **159**(4): 567-572.

Kupfer, D. J., Frank, E., Grochocinski, V. J., Houck, P. R. and Brown, C. (2005). African-American participants in a bipolar disorder registry: clinical and treatment characteristics. *Bipolar disorders* **7**(1): 82-88.

Lasser, K. E., Himmelstein, D. U., Woolhandler, S. J., McCormick, D. and Bor, D. H. (2002). Do minorities in the United States receive fewer mental health services than whites? *International journal of health services* **32**(3): 567-578.

Lawson, W., Johnston, S., Karson, C., Offord, S., Docherty, J., Eramo, A., Kamat, S., Blanchette, C. M., Carson, W. and Nasrallah, H. A. (2015). Racial differences in antipsychotic use: Claims database analysis of Medicaid-insured patients with schizophrenia. *Annals of clinical psychiatry* **27**(4): 242-252.

Lehman, A. F. and Steinwachs, D. M. (1998). Patterns of usual care for schizophrenia: initial results from the Schizophrenia Patient Outcomes Research Team (PORT) Client Survey. *Schizophrenia bulletin* **24**(1): 11-20; discussion 20-32.

Lelliott, P., C. Paton, M. Harrington, M. Konsolaki, T. Sensky, and C. Okocha (2002). The influence of patient variables on polypharmacy and combined high dose of antipsychotic drugs prescribed for in-patients. *Psychiatric bulletin* **26**: 411-414.

Leslie, D. L. and Rosenheck, R. (2012). Off-label use of antipsychotic medications in Medicaid. *American journal of managed care* **18**(3): e109-117.

Leslie, D. L. and Rosenheck, R. A. (2001). Use of pharmacy data to assess quality of pharmacotherapy for schizophrenia in a national health care system: individual and facility predictors. *Medical care* **39**(9): 923-933.

Leslie, D. L. and Rosenheck, R. A. (2004). Adherence of schizophrenia pharmacotherapy to published treatment recommendations: patient, facility, and provider predictors. *Schizophrenia bulletin* **30**(3): 649-658.

Leslie, L. K., Weckerly, J., Landsverk, J., Hough, R. L., Hurlburt, M. S. and Wood, P. A. (2003). Racial/ethnic differences in the use of psychotropic medication in high-risk children and adolescents. *Journal of the American Academy of Child and Adolescent Psychiatry* **42**(12): 1433-1442.

Lesser, I. M., Castro, D. B., Gaynes, B. N., Gonzalez, J., Rush, A. J., Alpert, J. E., Trivedi, M., Luther, J. F. and Wisniewski, S. R. (2007). Ethnicity/race and outcome in the treatment of depression: results from STAR*D. *Medical care* **45**(11): 1043-1051.

Lesser, I. M., Myers, H. F., Lin, K. M., Bingham Mira, C., Joseph, N. T., Olmos, N. T., Schettino, J. and Poland, R. E. (2010). Ethnic differences in antidepressant response: a prospective multi-site clinical trial. *Depression and anxiety* **27**(1): 56-62.

Leucht, S., Cipriani, A., Spineli, L., Mavridis, D., Orey, D., Richter, F., Samara, M., Barbui, C., Engel, R. R., Geddes, J. R., Kissling, W., Stapf, M. P., Lassig, B., Salanti, G. and Davis, J. M. (2013). Comparative efficacy and tolerability of 15 antipsychotic drugs in schizophrenia: a multiple-treatments meta-analysis. *Lancet (London, England)* **382**(9896): 951-962.

Leucht, S., Corves, C., Arbter, D., Engel, R. R., Li, C. and Davis, J. M. (2009). Second-generation versus first-generation antipsychotic drugs for schizophrenia: a meta-analysis. *Lancet (London, England)* **373** (9567): 31-41.

Lewis, G. and Appleby, L. (1988). Personality disorder: the patients psychiatrists dislike. *British journal of psychiatry* **153**: 44-49.

Lewis, G., Croft-Jeffreys, C. and David, A. (1990). Are British psychiatrists racist? *British journal of psychiatry* **157**: 410-415.

Lieberman, J. A., Stroup, T. S., McEvoy, J. P., Swartz, M. S., Rosenheck, R. A., Perkins, D. O., Keefe, R. S., Davis, S. M., Davis, C. E., Lebowitz, B. D., Severe, J. and Hsiao, J. K. (2005). Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. *New England journal of medicine* **353**(12): 1209-1223.

Lillie-Blanton, M., Brodie, M., Rowland, D., Altman, D. and McIntosh, M. (2000). Race, ethnicity, and the health care system: public perceptions and experiences. *Medical care research and review* **57 Suppl 1**: 218-235.

Lin, K. M. and Finder, E. (1983). Neuroleptic dosage for Asians. *The American journal of psychiatry* **140**(4): 490-491.

Lin, K. M., Matsuda, A. and Nuccio, I. (1996). Neuroleptic dosage in psychiatric outpatients. *Psychiatric services* **47**(5): 536.

Linares, L. O., Martinez-Martin, N. and Castellanos, F. X. (2013). Stimulant and atypical antipsychotic medications for children placed in foster homes. *PloS one* **8**(1): e54152.

Littlewood, R. and Cross, S. (1980). Ethnic minorities and psychiatric services. *Sociology of health & illness* **2**(2): 194-201.

Lloyd, K. and Moodley, P. (1992). Psychotropic medication and ethnicity: an inpatient survey. *Social psychiatry and psychiatric epidemiology* **27**(2): 95-101.

Lumley, T., Diehr, P., Emerson, S. and Chen, L. (2002). The importance of the normality assumption in large public health data sets. *Annual review of public health* **23**: 151-169.

Luo, R. D., Belleti, D. A., Tran, D., Arcona, S. and Salen, P. N. (2002). National prescribing patterns in the management of extrapyramidal symptoms among patients with schizophrenia. *International journal of psychiatry in medicine* **32**(3): 261-269.

Mace, S. and Taylor, D. (2005). A prescription survey of antipsychotic use in England and Wales following the introduction of NICE guidance. *International journal of psychiatry in clinical practice* **9**(2): 124-129.
Mace, S. and Taylor, D. (2015). Reducing the rates of prescribing high-dose antipsychotics and polypharmacy on psychiatric inpatient and intensive care units: results of a 6-year quality improvement programme. *Therapeutic advances in psychopharmacology* **5(1)**: 4–12.
MacEachern, S. (2011). *The concept of race in contemporary anthropology. In Race and ethnicity: the United States and the world.* 2nd Ed. New York, Prentice Hall.
Macpherson, W. (1999). *The Stephen Lawrence inquiry. Report of an inquiry by Sir William Macpherson of Cluny.* London, Stationery Office.
Mahy, G. E., Mallett, R., Leff, J. and Bhugra, D. (1999). First-contact incidence rate of schizophrenia on Barbados. *British journal of psychiatry* **175**(28-33).
Mallinger, J. B., Fisher, S. G., Brown, T. and Lamberti, J. S. (2006). Racial disparities in the use of second-generation antipsychotics for the treatment of schizophrenia. *Psychiatric services* **57**(1): 133-136.
Mann, F., Fisher, H. L., Major, B., Lawrence, J., Tapfumaneyi, A., Joyce, J., Hinton, M. F. and Johnson, S. (2014). Ethnic variations in compulsory detention and hospital admission for psychosis across four UK Early Intervention Services. *BMC psychiatry* **14**(1): 256.
Manuel, J. I., Essock, S. M., Wu, Y., Pangilinan, M. and Stroup, S. (2012). Factors associated with initiation on clozapine and on other antipsychotics among Medicaid enrollees. *Psychiatric services* **63**(11): 1146-1149.
Marconi, A., Di Forti, M., Lewis, C. M., Murray, R. M. and Vassos, E. (2016). Meta-analysis of the Association Between the Level of Cannabis Use and Risk of Psychosis. *Schizophrenia bulletin* **42(5)**: 1262-1269.
Mark, T. L., Palmer, L. A., Russo, P. A. and Vasey, J. (2003). Examination of treatment pattern differences by race. *Mental health services research* **5**(4): 241-250.
Marmot, M. (2001). From Black to Acheson: two decades of concern with inequalities in health. A celebration of the 90th birthday of Professor Jerry Morris. *International journal of epidemiology* **30**(5): 1165-1171.
Marmot, M. (2010). *Fair Society, Healthy Lives: A Strategic Review of Inequalities in England.* London, University College London.
Marmot, M. G., Smith, G. D., Stansfeld, S., Patel, C., North, F., Head, J., White, I., Brunner, E. and Feeney, A. (1991). Health inequalities among British civil servants: the Whitehall II study. *Lancet (London, England)* **337**(8754): 1387-1393.
Mathur, R., Bhaskaran, K., Chaturvedi, N., Leon, D. A., vanStaa, T., Grundy, E., Smeeth, L., (2014). Completeness and usability of ethnicity data in UK-based primary care and hospital databases. *Journal of public health* **36**(4): 684-692.
Mathur, R., Grundy, E., Smeeth, L., (2013). *Availability and use of UK based ethnicity data for health research.*, National Centre for Research Methods.
Matsuda, K. T., Cho, M. C., Lin, K. M., Smith, M. W., Young, A. S. and Adams, J. A. (1996). Clozapine dosage, serum levels, efficacy, and side-effect profiles: a comparison of Korean-American and Caucasian patients. *Psychopharmacology bulletin* **32**(2): 253-257.
Mays, V. M. (1985). The Black American and psychotherapy: The dilemma. *Psychotherapy* **22**(2S): 379.

McCallum, J. M., Arekere, D. M., Green, B. L., Katz, R. V. and Rivers, B. M. (2006). Awareness and knowledge of the U.S. Public Health Service syphilis study at Tuskegee: implications for biomedical research. *Journal of health care for the poor and underserved* **17**(4): 716-733.

McCutcheon, R., Beck, K., Bloomfield, M. A., Marques, T. R., Rogdaki, M. and Howes, O. D. (2015). Treatment resistant or resistant to treatment? Antipsychotic plasma levels in patients with poorly controlled psychotic symptoms. *Journal of psychopharmacology* **29**(8): 892-897.

McGraw, J. and Waller, D. (2012). Cytochrome P450 variations in different ethnic populations. *Expert opinion on drug metabolism & toxicology* **8**(3): 371-382.

McKenzie, K. and Bhui, K. (2007). Institutional racism in mental health care. *British medical journal* **334**(7595): 649-650.

McKenzie, K., Samele, C., Van Horn, E., Tattan, T., Van Os, J. and Murray, R. (2001). Comparison of the outcome and treatment of psychosis in people of Caribbean origin living in the UK and British Whites. Report from the UK700 trial. *British journal of psychiatry* **178**: 160-165.

McKenzie, K., van Os, J., Fahy, T., Jones, P., Harvey, I., Toone, B. and Murray, R. (1995). Psychosis with good prognosis in Afro-Caribbean people now living in the United Kingdom. *British medical journal* **311**(7016): 1325-1328.

Melba, M. (2010). *Delivering Race Equality Action Plan: a five year review*, Department of Health.

Meltzer, H. Y., Bobo, W. V., Roy, A., Jayathilake, K., Chen, Y., Ertugrul, A., Anil Yagcioglu, A. E. and Small, J. G. (2008). A randomized, double-blind comparison of clozapine and high-dose olanzapine in treatment-resistant patients with schizophrenia. *Journal of clinical psychiatry* **69**(2): 274-285.

Metcalfe, S., Laking, G. and Arnold, J. (2013). Variation in the use of medicines by ethnicity during 2006/07 in New Zealand: a preliminary analysis. *New Zealand medical journal* **126**(1384): 14-41.

Meyer, N., Gee, S., Whiskey, E., Taylor, D., Mijovic, A., Gaughran, F., Shergill, S. and MacCabe, J. H. (2015). Optimizing Outcomes in Clozapine Rechallenge Following Neutropenia: A Cohort Analysis. *Journal of clinical psychiatry* **76**(11): 1410-1416.

Minnis, H., McMillan, A., Gillies, M. and Smith, S. (2001). Racial stereotyping: survey of psychiatrists in the United Kingdom. *British medical journal* **323**(7318): 905-906.

Monthly Index of Medical Specialities (December 2008). London, Haymarket Medical Media.

Moore, S., Jaime, L. K., Maharajh, H., Ramtahal, I., Reid, S., Ramsewak, F. S. and Maharaj, M. (2002). The prescribing of psychotropic drugs in mental health services in Trinidad. *Pan American journal of public health* **12**(3): 207-214.

Moore, T. J. and Mattison, D. R. (2017). Adult Utilization of Psychiatric Drugs and Differences by Sex, Age, and Race. *JAMA internal medicine* **177**(2): 274-275.

Morgan, C., Dazzan, P., Morgan, K., Jones, P., Harrison, G., Leff, J., Murray, R. and Fearon, P. (2006). First episode psychosis and ethnicity: initial findings from the AESOP study. *World psychiatry : official journal of the World Psychiatric Association (WPA)* **5**(1): 40-46.

Morrato, E. H., Dodd, S., Oderda, G., Haxby, D. G., Allen, R. and Valuck, R. J. (2007). Prevalence, utilization patterns, and predictors of antipsychotic polypharmacy: experience in a multistate Medicaid population, 1998-2003. *Clinical therapeutics* **29**(1): 183-195.

Mrazek, D. A. (2010). Psychiatric pharmacogenomic testing in clinical practice. *Dialogues in clinical neuroscience* **12**(1): 69-76.
Mukherjee, S., Shukla, S., Woodle, J., Rosen, A. M. and Olarte, S. (1983). Misdiagnosis of schizophrenia in bipolar patients: A multiethnic comparison. *American journal of psychiatry* **140**(12): 1571-1574.
Murray, M. (2006). Role of CYP pharmacogenetics and drug-drug interactions in the efficacy and safety of atypical and other antipsychotic agents. *Journal of pharmacy and pharmacology* **58**(7): 871-885.
Murray, R. and Fearon, P. (2007). Searching for racists under the psychiatric bed: Commentary on... Institutional racism in psychiatry. *Psychiatrist* **31**(10): 365-366.
Murthy, V. H., Krumholz, H. M. and Gross, C. P. (2004). Participation in cancer clinical trials: Race-, sex-, and age-based disparities. *Journal of the American Medical Association* **291**(22): 2720-2726.
Nair, C. S. and Adams, P. (2009). Survey Platform: A Factor Influencing Online Survey Delivery and Response Rate. *Quality in higher education* **15**(3): 291-296.
National Institute for Health and Care Excellence (2015). *Violence and Agression. Short-term management in mental health, health and community settings*. [Online]. Available from: http://www.nice.org.uk/guidance/ng10/evidence/full-guideline-60711085 accessed 20th January 2016.
National Institutes of Health (1993). National Institutes of Health Revitalization Act.
National Institutes of Health (2001). NIH Policy and Guidelines on The Inclusion of Women and Minorities as Subjects in Clinical Research.
Nazroo, J. (1997). *Ethnicity & mental health. Findings from a national community survey*. London, Policy Studies Institute.
Nazroo, J. Y. (1998). Rethinking the relationship between ethnicity and mental health: the British Fourth National Survey of Ethnic Minorities. *Social psychiatry and psychiatric epidemiology* **33**(4): 145-148.
Neighbors, H., Jackson, J., Campbell, L. and Williams, D. (1989). The influence of racial factors on psychiatric diagnosis: a review and suggestions for research. *Community mental health journal* **25**(4): 301-311.
Nejtek, V. A., Allison, N. and Hilburn, C. (2012). Race- and gender-related differences in clinical characteristics and quality of life among outpatients with psychotic disorders. *Journal of psychiatric practice* **18**(5): 329-337.
Newman, P. A., Duan, N., Roberts, K. J., Seiden, D., Rudy, E. T., Swendeman, D. and Popova, S. (2006). HIV Vaccine Trial Participation Among Ethnic Minority Communities: Barriers, Motivators, and Implications for Recruitment. *Journal of acquired immune deficiency syndromes* **41**(2): 210-217.
Ng, C. H., Chong, S. A., Lambert, T., Fan, A., Hackett, L. P., Mahendran, R., Subramaniam, M. and Schweitzer, I. (2005). An inter-ethnic comparison study of clozapine dosage, clinical response and plasma levels. *International clinical psychopharmacology* **20**(3): 163-168.
NHS Centre for Reviews and Dissemination (1996). Ethnicity and health: Reviews of literature and guidance for purchasers in the areas of cardiovascular disease, mental health and haemoglobinopathies.
Nielsen, J., Dahm, M., Lublin, H. and Taylor, D. (2010). Psychiatrists' attitude towards and knowledge of clozapine treatment. *Journal of psychopharmacology* **24(7)**: 965-971.
Norfolk Suffolk & Cambridgeshire Strategic Health Authority (2003). Independent Inquiry into the death of David Bennett.

Nose, M., Tansella, M., Thornicroft, G., Schene, A., Becker, T., Veronese, A., Leese, M., Koeter, M., Angermeyer, M. and Barbui, C. (2008). Is the Defined Daily Dose system a reliable tool for standardizing antipsychotic dosages? *International clinical psychopharmacology* **23**(5): 287-290.

Novick, D., Haro, J. M., Suarez, D., Perez, V., Dittmann, R. W. and Haddad, P. M. (2010). Predictors and clinical consequences of non-adherence with antipsychotic medication in the outpatient treatment of schizophrenia. *Psychiatry research* **176**(2): 109-113.

Nulty, D. D. (2008). The adequacy of response rates to online and paper surveys: what can be done? *Assessment and valuation in higher education* **33**(3): 301-314.

Ødegaard, Ø. (1932). *Emigration and insanity: a study of mental disease among the Norwegianborn population of Minnesota*. Copenhagen : Levin & Munksgaard.

Oesterheld, J. R. (2009). *2D6 in Clinical Manual of Drug Interaction. Principles for Medical Practice*. Washington DC, American Psychiatric Publishing Inc.

Office for National Statistics (2001). Ethnic group statistics

Office for National Statistics (2003). Ethnic group statistics: A guide for the collection and classification of ethnicity data.

Office for National Statistics (2006). A guide to comparing 1991and 2001 Census ethnic group data.

Office for National Statistics (2011). Ethnicity and National Identity in England and Wales: 2011.

Office for National Statistics (2015). Harmonised Concepts and Questions for Social Data Sources. Primary Principles. Ethnic Group.

Olfson, M., Blanco, C., Liu, L., Moreno, C. and Laje, G. (2006). National trends in the outpatient treatment of children and adolescents with antipsychotic drugs. *Archives of general psychiatry* **63**(6): 679-685.

Opolka, J. L., Rascati, K. L., Brown, C. M., Barner, J. C., Johnsrud, M. T. and Gibson, P. J. (2003). Ethnic differences in use of antipsychotic medication among Texas medicaid clients with schizophrenia. *Journal of clinical psychiatry* **64**(6): 635-639.

Opolka, J. L., Rascati, K. L., Brown, C. M. and Gibson, P. J. (2004). Ethnicity and prescription patterns for haloperidol, risperidone, and olanzapine. *Psychiatric services* **55**(2): 151-156.

Owen, R. R., Feng, W., Thrush C.R. , Hudson T.J. and Austen M.A (2001). Variations in prescribing practices for novel antipsychotic medications among Veterans Affairs hospitals. *Psychiatric services* **52**: 1523-1525.

Owen, R. R., Fischer, E. P., Kirchner, J. E., Thrush, C. R., Williams, D. K., Cuffel, B. J., Elliott, C. E. and Booth, B. M. (2003). Clinical practice variations in prescribing antipsychotics for patients with schizophrenia. *American journal of medical quality* **18**(4): 140-146.

Parkman, S., Davies, S., Leese, M., Phelan, M. and Thornicroft, G. (1997). Ethnic differences in satisfaction with mental health services among representative people with psychosis in south London: PRiSM study 4. *British journal of psychiatry* **171**: 260-264.

Patel, M. X., Arista, I. A., Taylor, M. and Barnes, T. R. (2013). How to compare doses of different antipsychotics: a systematic review of methods. *Schizophrenia research* **149**(1-3): 141-148.

Patel, M. X., Bishara, D., Jayakumar, S., Zalewska, K., Shiers, D., Crawford, M. J. and Cooper, S. J. (2014). Quality of prescribing for schizophrenia: evidence from a

national audit in England and Wales. *European neuropsychopharmacology* **24**(4): 499-509.
Patel, N. C., DelBello, M. P., Keck, P. E., Jr. and Strakowski, S. M. (2005). Ethnic differences in maintenance antipsychotic prescription among adolescents with bipolar disorder. *Journal of child and adolescent psychopharmacology* **15**(6): 938-946.
Paton, C., Barnes, T. R., Cavanagh, M. R., Taylor, D., Lelliott, P. and Pomh-Uk project team (2008). High-dose and combination antipsychotic prescribing in acute adult wards in the UK: the challenges posed by p.r.n. prescribing. *British journal of psychiatry* **192**(6): 435-439.
Perera, V., Gross, A. S. and McLachlan, A. J. (2012). Influence of environmental and genetic factors on CYP1A2 activity in individuals of South Asian and European ancestry. *Clinical pharmacology and therapeutics* **92**(4): 511-519.
Perry, P. J. (2001). Therapeutic drug monitoring of antipsychotics. *Psychopharmacology bulletin* **35**(3): 19-29.
Peveler, R. C., Branford, D., Citrome, L., Fitzgerald, P., Harvey, P. W., Holt, R. I., Howard, L., Kohen, D., Jones, I., O'Keane, V., Pariente, C. M., Pendlebury, J., Smith, S. M. and Yeomans, D. (2008). Antipsychotics and hyperprolactinaemia: clinical recommendations. *Journal of psychopharmacology* **22**(2 Suppl): 98-103.
Pinninti, N. R., Shaila, B. and Kumar, G. (2003). Racial bias in the prescription atypical of antipsychotics? *Psychiatric services* **54**(1): 110.
Pinto, R., Ashworth, M., Seed, P., Rowlands, G., Schofield, P. and Jones, R. (2010). Differences in the primary care management of patients with psychosis from two ethnic groups: a population-based cross-sectional study. *Family practice* **27**(4): 439-446.
Pipe, R., Bhat, A., Matthews, B. and Hampstead, J. (1991). Section 136 and African/Afro-Caribbean minorities. *International journal of social psychiatry* **37**(1): 14-23.
Pogge, D. L., Young, K., Insalaco, B. and Harvey, P. D. (2007). Use of atypical antipsychotic medications in adolescent psychiatric inpatients: a comparison with inpatients who did not receive antipsychotic medications during their stay. *International journal of clinical practice* **61**(6): 896-902.
Ponto, T., Ismail, N. I., Abdul Majeed, A. B., Marmaya, N. H. and Zakaria, Z. A. (2010). A prospective study on the pattern of medication use for schizophrenia in the outpatient pharmacy department, Hospital Tengku Ampuan Rahimah, Selangor, Malaysia. *Methods and findings in experimental and clinical pharmacology* **32**(6): 427-432.
Preston, C. (2015). "*Stockley's Drug Interactions*." Available at: https://www.medicinescomplete.com/mc/stockley (Accessed: 4th February 2016).
Price, N., Glazer, W. and Morgenstern, H. (1985). Demographic predictors of the use of injectable versus oral antipsychotic medications in outpatients. *American journal of psychiatry* **142**(12): 1491-1492.
Prins, H. (1993). *Report of the Committee of Inquiry into the Death in Broadmoor Hospital of Orville Blackwood and a Review of the Deaths of Two Other Afro-Caribbean Patients: 'Big, Black and Dangerous?* London, Special Hospitals Service Authority.
Puyat, J. H., Daw, J. R., Cunningham, C. M., Law, M. R., Wong, S. T., Greyson, D. L. and Morgan, S. G. (2013). Racial and ethnic disparities in the use of

antipsychotic medication: a systematic review and meta-analysis. *Social psychiatry and psychiatric epidemiology* **48**(12): 1861-1872.
Puyat, J. H., Hanley, G. E., Cunningham, C. M., Law, M. R., Wong, S. T., Sutherland, J. M. and Morgan, S. G. (2011). Ethnic disparities in antipsychotic drug use in British Columbia: a cross-sectional retrospective study. *Psychiatric services* **62**(9): 1026-1031.
Ranganathan, M. and Bhopal, R. (2006). Exclusion and inclusion of nonwhite ethnic minority groups in 72 North American and European cardiovascular cohort studies. *PLoS medicine* **3**(3): e44.
Rathod, S., Kingdon, D., Phiri, P. and Gobbi, M. (2010). Developing culturally sensitive cognitive behaviour therapy for psychosis for ethnic minority patients by exploration and incorporation of service users' and health professionals' views and opinions. *Behavioural and cognitive psychotherapy* **38**(5): 511-533.
Rathod, S., Kingdon, D., Smith, P. and Turkington, D. (2005). Insight into schizophrenia: the effects of cognitive behavioural therapy on the components of insight and association with sociodemographics--data on a previously published randomised controlled trial. *Schizophrenia research* **74**(2-3): 211-219.
Rathore, S. S. and Krumholz, H. M. (2003). Race, ethnic group, and clinical research. *British medical journal* **327**(7418): 763-764.
Reid, D. D., Brett, G. Z., Hamilton, P. J., Jarrett, R. J., Keen, H. and Rose, G. (1974). Cardiorespiratory disease and diabetes among middle-aged male Civil Servants. A study of screening and intervention. *Lancet (London, England)* **1**(7856): 469-473.
Relling, M. V., Lin, J. S., Ayers, G. D. and Evans, W. E. (1992). Racial and gender differences in N-acetyltransferase, xanthine oxidase, and CYP1A2 activities. *Clinical pharmacology and therapeutics* **52**(6): 643-658.
Rijcken, C. A., Monster, T. B., Brouwers, J. R. and de Jong-van den Berg, L. T. (2003). Chlorpromazine equivalents versus defined daily doses: how to compare antipsychotic drug doses? *Journal of clinical psychopharmacology* **23**(6): 657-659.
Riolo, S. A., Nguyen, T. A., Greden, J. F. and King, C. A. (2005). Prevalence of depression by race/ethnicity: findings from the National Health and Nutrition Examination Survey III. *American journal of public health* **95**(6): 998-1000.
Ritchie, J., Donald, D. & Lingham, R., (1994). The Report of the Inquiry into the Care and Treatment of Christopher Clunis by Jean Ritchie, Donald Dick and Richard Lingham.
Robst, J. (2012). Changes in antipsychotic medication use after implementation of a Medicaid mental health carve-out in the US. *PharmacoEconomics* **30**(5): 387-396.
Rochon, P. A., Mashari, A., Cohen, A., Misra, A., Laxer, D., Streiner, D. L., Clark, J. P., Dergal, J. M. and Gold, J. (2004). The inclusion of minority groups in clinical trials: problems of under representation and under reporting of data. *Accountability in research* **11**(3-4): 215-223.
Rodday, A. M., Parsons, S. K., Correll, C. U., Robb, A. S., Zima, B. T., Saunders, T. S. and Leslie, L. K. (2014). Child and adolescent psychiatrists' attitudes and practices prescribing second generation antipsychotics. *Journal of child and adolescent psychopharmacology* **24**(2): 90-93.
Rost, K., Hsieh, Y. P., Xu, S., Menachemi, N. and Young, A. S. (2011). Potential disparities in the management of schizophrenia in the United States. *Psychiatric services* **62**(6): 613-618.

Ruiz, P., Varner, R. V., Small, D. R. and Johnson, B. A. (1999). Ethnic differences in the neuroleptic treatment of schizophrenia. *Psychiatric quarterly* **70**(2): 163-172.

Ruiz, S., Chu, P., Sramek, J., Rotavu, E. and Herrera, J. (1996). Neuroleptic dosing in Asian and Hispanic outpatients with schizophrenia. *Mount Sinai journal of medicine* **63**(5-6): 306-309.

Rummel-Kluge, C., Komossa, K., Schwarz, S., Hunger, H., Schmid, F., Lobos, C. A., Kissling, W., Davis, J. M. and Leucht, S. (2010). Head-to-head comparisons of metabolic side effects of second generation antipsychotics in the treatment of schizophrenia: a systematic review and meta-analysis. *Schizophrenia research* **123**(2-3): 225-233.

Sander, A. M., Pappadis, M. R., Davis, L. C., Clark, A. N., Evans, G., Struchen, M. A. and Mazzei, D. M. (2009). Relationship of race/ethnicity and income to community integration following traumatic brain injury: investigation in a non-rehabilitation trauma sample. *Neurorehabilitation* **24**(1): 15-27.

Sashidharan, S. (1993). Afro-Caribbeans and schizophrenia: the ethnic vulnerability hypothesis re-examined. *International review of psychiatry* **5**(2-3): 129-144.

Sashidharan, S. P. and Francis, E. (1999). Racism in psychiatry necessitates reappraisal of general procedures and Eurocentric theories. *British medical journal* **319**(7204): 254.

Saunders, C. L., Abel, G. A., El Turabi, A., Ahmed, F. and Lyratzopoulos, G. (2013). Accuracy of routinely recorded ethnic group information compared with self-reported ethnicity: evidence from the English Cancer Patient Experience survey. *British medical journal* **3**(6): 1-8.

Schwartz, R. C. and Blankenship, D. M. (2014). Racial disparities in psychotic disorder diagnosis: A review of empirical literature. *World journal of psychiatry* **4**(4): 133-140.

Segal, S. P., Bola, J. R. and Watson, M. A. (1996). Race, quality of care, and antipsychotic prescribing practices in psychiatric emergency services. *Psychiatric services* **47**(3): 282-286.

Selten, J. P., Cantor-Graae, E., Slaets, J. and Kahn, R. S. (2002). Odegaard's selection hypothesis revisited: schizophrenia in Surinamese immigrants to The Netherlands. *American journal of psychiatry* **159**(4): 669-671.

Selten, J. P., Veen, N., Feller, W., Blom, J. D., Schols, D., Camoenie, W., Oolders, J., van der Velden, M., Hoek, H. W., Rivero, V. M., van der Graaf, Y. and Kahn, R. (2001). incidence of psychotic disorders in immigrant groups to The Netherlands. *British journal of psychiatry* **178(4)**: 367-372.

Senior, P. A. and Bhopal, R. (1994). Ethnicity as a variable in epidemiological research. *British medical journal* **309**(6950): 327-330.

Sharpley, M., Hutchinson, G., McKenzie, K. and Murray, R. M. (2001). Understanding the excess of psychosis among the African-Caribbean population in England. Review of current hypotheses. *British journal of psychiatry. Supplement* **40**: s60-68.

Shavers, V. L., Lynch, C. F. and Burmeister, L. F. (2002). Racial Differences in Factors that Influence the Willingness to Participate in Medical Research Studies. *Annals of epidemiology* **12**(4): 248-256.

Shea, M. and Yeh, C. J. (2008). Asian American students' cultural values, stigma, and relational self-construal: Correlates of attitudes toward professional help seeking. *Journal of mental health counseling* **30**(2): 157.

Shi, L., Ascher-Svanum, H., Zhu, B., Faries D., Montgomery W. and Marder S.R. (2007). Characteristics and use patterns of patients taking first-generation depot antipsychotics or oral antipsychotics for schizophrenia. *Psychiatric services* **58**: 482-488.

Shim, J. C., Shin, J. G., Kelly, D. L., Jung, D. U., Seo, Y. S., Liu, K. H., Shon, J. H. and Conley, R. R. (2007). Adjunctive treatment with a dopamine partial agonist, aripiprazole, for antipsychotic-induced hyperprolactinemia: a placebo-controlled trial. *American journal of psychiatry* **164**(9): 1404-1410.

Shubsachs, A. P., Huws, R. W., Close, A. A., Larkin, E. P. and Falvey, J. (1995). Male Afro-Caribbean patients admitted to Rampton Hospital between 1977 and 1986--a control study. *Medicine, science, and the law* **35**(4): 336-346.

Singh, S. (2007). Institutional racism in psychiatry: lessons from inquiries. *Psychiatric bulletin* **31**: 363-365.

Singh, S. P. and Burns, T. (2006). Race and mental health: there is more to race than racism. *British medical journal* **333**(7569): 648-651.

Sleath, B., Domino, M. E., Wiley-Exley, E., Martin, B., Richards, S. and Carey, T. (2010). Antidepressant and antipsychotic use and adherence among Medicaid youths: differences by race. *Community mental health journal* **46**(3): 265-272.

Sleath, B. L., Rubin, R. H. and Huston, S. A. (2001). Antidepressant prescribing to Hispanic and non-Hispanic white patients in primary care. *Annals of pharmacotherapy* **35**(4): 419-423.

Smart, A., Tutton, R., Martin, P., Ellison, G. T. and Ashcroft, R. (2008). The standardization of race and ethnicity in biomedical science editorials and UK biobanks. *Social studies of science* **38**(3): 407-423.

Sohler, N. L., Bromet, E. J., Lavelle, J., Craig, T. J. and Mojtabai, R. (2004). Are there racial differences in the way patients with psychotic disorders are treated at their first hospitalization? *Psychological medicine* **34**(4): 705-718.

South London and Maudsley NHS Trust (2005). *Race Equality Scheme and Action Plan 2005-2008*.

Sparshatt, A., Taylor, D., Patel, M. X. and Kapur, S. (2010). A systematic review of aripiprazole--dose, plasma concentration, receptor occupancy, and response: implications for therapeutic drug monitoring. *Journal of clinical psychiatry* **71**(11): 1447-1456.

Sprotson K, N. J. (2002). *Ethnic Minority Psychiatric Illness Rates in the Community (EMPIRIC) - Quantitative Report*. London, National Centre for Social Research and the Department of Epidemiology and Public Health at the Royal Free and University College Medical School.

Staller, J. A., Wade, M. J. and Baker, M. (2005). Current prescribing patterns in outpatient child and adolescent psychiatric practice in central New York. *Journal of child and adolescent psychopharmacology* **15**(1): 57-61.

Stanley, A. K. and Doyle, M. A. (1993). Audit of above BNF dosage medication. *Psychiatrist* **17**(5): 299-300.

Sterne, J. A., White, I. R., Carlin, J. B., Spratt, M., Royston, P., Kenward, M. G., Wood, A. M. and Carpenter, J. R. (2009). Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. *British medical journal* **338**: b2393.

Stevenson, D. G., Decker, S. L., Dwyer, L. L., Huskamp, H. A., Grabowski, D. C., Metzger, E. D. and Mitchell, S. L. (2010). Antipsychotic and benzodiazepine use among nursing home residents: findings from the 2004 National Nursing Home Survey. *American journal of geriatric psychiatry* **18**(12): 1078-1092.

Stewart, J. H., Bertoni, A. G., Staten, J. L., Levine, E. A. and Gross, P. C. (2007). Participation in Surgical Oncology Clinical Trials: Gender-, Race/Ethnicity-, and Age-based Disparities. *Annals of surgical oncology* **14**(12): 3328-3334.

Storch, D. D. and Storch, E. A. (1998). Racial disparity in medications prescribed. *Journal of the American Academy of Child & Adolescent Psychiatry* **37**(12): 1241-1242.

Strakowski, S. M., Shelton, R. C. and Kolbrener, M. L. (1993). The effects of race and comorbidity on clinical diagnosis in patients with psychosis. *Journal of clinical psychiatry* **54**(3): 96-102.

Stroup, T. S., Gerhard, T., Crystal, S., Huang, C. and Olfson, M. (2014). Geographic and clinical variation in clozapine use in the United States. *Psychiatric services* **65**(2): 186-192.

Stroup, T. S., Lieberman, J. A., McEvoy, J. P., Swartz, M. S., Davis, S. M., Rosenheck, R. A., Perkins, D. O., Keefe, R. S., Davis, C. E., Severe, J. and Hsiao, J. K. (2006). Effectiveness of olanzapine, quetiapine, risperidone, and ziprasidone in patients with chronic schizophrenia following discontinuation of a previous atypical antipsychotic. *American journal of psychiatry* **163**(4): 611-622.

Stubbs, J., Haw, C. and Taylor, D. (2006). Prescription errors in psychiatry–a multi-centre study. *Journal of psychopharmacology* **20**(4): 553-561.

Swan, J., Lillis, S. and Simmons, D. (2006). Investigating the accuracy of ethnicity data in New Zealand hospital records: still room for improvement. *New Zealand medical journal* **119**(1239): U2103.

Swanson, G. M. and Ward, A. J. (1995). Recruiting minorities into clinical trials: toward a participant-friendly system. *Journal of the National Cancer Institute* **87**(23): 1747-1759.

Szarek, B. L. and Goethe, J. W. (2003). Racial differences in use of antipsychotics among patients with bipolar disorder. *Journal of clinical psychiatry* **64**(5).

Takeshita, J., Goebert, D., Else, I., Carlton, B., Matsu, C. and Guerrero, A. (2014). Atypical antipsychotic usage among Asian Americans and Pacific Islanders. *Hawai'i journal of medicine & public health* **73**(9): 288-291.

Tamayo, J. M., Mazzotti, G., Tohen, M., Gattaz, W. F., Zapata, R., Castillo, J. J., Fahrer, R. D., González-Pinto, A. M., Vieta, E. and Azorin, J. M. (2007). Outcomes for Latin American versus White patients suffering from acute mania in a randomized, double-blind trial comparing olanzapine and haloperidol. *Journal of clinical psychopharmacology* **27**(2): 126-134.

Tang, Y., Horvitz-Lennon, M., Gellad, W. F., Lave, J. R., Chang, C. H., Normand, S. L. and Donohue, J. M. (2017). Prescribing of Clozapine and Antipsychotic Polypharmacy for Schizophrenia in a Large Medicaid Program. *Psychiatric services* **68**(6): 579-586.

Taylor, D. (1997). Switching from typical to atypical antipsychotics. *CNS drugs* **8**(4): 285-292.

Taylor, D., Mir, S., Mace, S. and Whiskey, E. (2002). Co-prescribing of atypical and typical antipsychotics—prescribing sequence and documented outcome. *Psychiatrist* **26**(5): 170-172.

Taylor, D., Paton, C. and Kapur, S. (2015). *The Maudsley Prescribing Guidelines in Psychiatry*. Chichester, Wiley Blackwell.

Taylor, D., Shapland, L., Laverick, G., Bond, J. and Munro, J. (2000). Clozapine - a survey of patient perceptions. *Psychiatric bulletin* **24**(12): 450-452.

Taylor, D. M. (2004). Prescribing of clozapine and olanzapine: dosage, polypharmacy and patient ethnicity. *Psychiatrist* **28(7)**: 241-243.

Taylor, D. M. and Smith, L. (2009). Augmentation of clozapine with a second antipsychotic--a meta-analysis of randomized, placebo-controlled studies. *Acta psychiatrica Scandinavica* **119**(6): 419-425.
Taylor, D. M., Young, C. and Paton, C. (2003). Prior antipsychotic prescribing in patients currently receiving clozapine: a case note review. *Journal of clinical psychiatry* **64**(1): 30-34.
Teo, C., Borlido, C., Kennedy, J. L. and De Luca, V. (2013). The role of ethnicity in treatment refractory schizophrenia. *Comprehensive psychiatry* **54**(2): 167-172.
The European Parliament (2014). Clinical Trials Regulation (EU) No 536/2014 of the European Parliment and of the Council of 16th April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC.
Thompson, A., Sullivan, S., Barley, M., Strange, S., Moore, L., Rogers, P., Sipos, A. and Harrison, G. (2008). The DEBIT trial: an intervention to reduce antipsychotic polypharmacy prescribing in adult psychiatry wards–a cluster randomized controlled trial. *Psychological medicine* **38**(05): 705-715.
Thompson, E. E., Neighbors, H. W., Munday, C. and Jackson, J. S. (1996). Recruitment and retention of African American patients for clinical research: an exploration of response rates in an urban psychiatric hospital. *Journal of consulting and clinical psychology* **64**(5): 861-867.
Thompson, J. V., Clark, J. M., Legge, S. E., Kadra, G., Downs, J., Walters, J. T., Hamshere, M. L., Hayes, R. D., Taylor, D. and MacCabe, J. H. (2016). Antipsychotic polypharmacy and augmentation strategies prior to clozapine initiation: a historical cohort study of 310 adults with treatment-resistant schizophrenic disorders. *Journal of psychopharmacology* **30(5)**: 436-443.
Thompson, V. L. and Alexander, H. (2006). Therapists' race and African American clients' reactions to therapy. *Psychotherapy* **43**(1): 99-110.
Thorens, G., Gex-Fabry, M., Zullino, D. F. and Eytan, A. (2008). Attitudes toward psychopharmacology among hospitalized patients from diverse ethno-cultural backgrounds. *BMC psychiatry* **8**(1): 55.
Townsend, P., Davidson, N, Whitehead, M (eds). (1992). *Inequalities in Health: The Black Report; The Health Divide*. London, Pelican Books.
Trierweiler, S. J., Neighbors, H. W., Munday, C., Thompson, E. E., Jackson, J. S. and Binion, V. J. (2006). Differences in patterns of symptom attribution in diagnosing schizophrenia between African American and non-African American clinicians. *American journal of orthopsychiatry* **76**(2): 154-160.
Tunnicliffe, S., Harrison, G. and Standen, P. J. (1992). Factors affecting compliance with depot injection treatment in the community. *Social psychiatry and psychiatric epidemiology* **27**(5): 230-233.
UK Drug Policy Commission (2010). *Drugs and Diversity: Ethnic minority groups*.
United Nations Educational Scientific and Cultural Organiszation (1950). The Race Question.
University of Leeds (2015). *Clearing House for Postgraduate Course in Clinical Psychology*.
Valenstein, M., Copeland, L., Owen, R., Blow, F. and Visnic, S. (2001a). Delays in adopting evidence-based dosages of conventional antipsychotics. *Psychiatric services* **52**(9): 1242-1244.
Valenstein, M., Copeland, L. A., Owen, R., Blow, F. C. and Visnic, S. (2001b). Adherence assessments and the use of depot antipsychotics in patients with schizophrenia. *Journal of clinical psychiatry* **62**(7): 545-551.

Valenstein, M., McCarthy, J. F., Ignacio, R. V., Dalack, G. W., Stavenger, T. and Blow, F. C. (2006). Patient- and facility-level factors associated with diffusion of a new antipsychotic in the VA health system. *Psychiatric services* **57**(1): 70-76.

Valenti, A. M., Narendran, R. and Pristach, C. A. (2003). Who are patients on conventional antipsychotics? *Schizophrenia bulletin* **29**(2): 195-199.

Van Dorn, R. A., Swanson, J. W., Swartz, M. S. and Elbogen, E. B. (2005). The effects of race and criminal justice involvement on access to atypical antipsychotic medications among persons with schizophrenia. *Mental health services research* **7**(2): 123-134.

Van, O. J., Castle, D. J., Takei, N., Der, G. and Murray, R. M. (1996). Psychotic illness in ethnic minorities: clarification from the 1991 census. *Psychological medicine* **26**(1): 203-208.

van Ryn, M. and Burke, J. (2000). The effect of patient race and socio-economic status on physicians' perceptions of patients. *Social science & medicine* **50**(6): 813-828.

Variations Sub-group of the Chief Medical Officer's Health of the Nation Working Group (1996). *Variations in Health: What Can the Department of Health and the NHS do*, Department of Health.

Varner, R. V., Hays, J. R., Wagner, A. L. and Averill, P. (2001). Outcome comparison of patients receiving oral or depot neuroleptic medication. *Psychological reports* **89**(1): 169-174.

Veen, N., Selten, J. P., Hoek, H., Feller, W., Van der Graaf, Y. and Kahn, R. (2002). Use of illicit substances in a psychosis incidence cohort: a comparison among different ethnic groups in the Netherlands. *Acta psychiatrica Scandinavica* **105**(6): 440-443.

Velligan, D. I., Carroll, C., Lage, M. J. and Fairman, K. (2015). Outcomes of medicaid beneficiaries with schizophrenia receiving clozapine only or antipsychotic combinations. *Psychiatric services* **66**(2): 127-133.

Waddington, J. L., Youssef, H. A. and Kinsella, A. (1998). Mortality in schizophrenia. Antipsychotic polypharmacy and absence of adjunctive anticholinergics over the course of a 10-year prospective study. *British journal of psychiatry* **173**: 325-329.

Waldman, S. V., Blumenthal, J. A., Babyak, M. A., Sherwood, A., Sketch, M., Davidson, J. and Watkins, L. L. (2009). Ethnic differences in the treatment of depression in patients with ischemic heart disease. *American heart journal* **157**(1): 77-83.

Waldo, D. R. (2004). Accuracy and Bias of Race/Ethnicity Codes in the Medicare Enrollment Database. *Health care financing review* **26**(2): 61-72.

Walkup, J. T., McAlpine, D. D., Olfson, M., Labay, L. E., Boyer, C. and Hansell, S. (2000). Patients with schizophrenia at risk for excessive antipsychotic dosing. *Journal of clinical psychiatry* **61**(5): 344-348.

Walters, P., Ashworth, M. and Tylee, A. (2008). Ethnic density, physical illness, social deprivation and antidepressant prescribing in primary care: ecological study. *British journal of psychiatry* **193**(3): 235-239.

Wandel, C., Witte, J. S., Hall, J. M., Stein, C. M., Wood, A. J. and Wilkinson, G. R. (2000). CYP3A activity in African American and European American men: population differences and functional effect of the CYP3A4*1B5'-promoter region polymorphism. *Clinical pharmacology and therapeutics* **68**(1): 82-91.

Wang, P. S., West, J. C., Tanielian, T. and Pincus, H. A. (2000). Recent patterns and predictors of antipsychotic medication regimens used to treat schizophrenia and other psychotic disorders. *Schizophrenia bulletin* **26**(2): 451-457.

Webb, R., Richardson, J., Esmail, A. and Pickles, A. (2004). Uptake for cervical screening by ethnicity and place-of-birth: a population-based cross-sectional study. *Journal of public health* **26**(3): 293-296.

Wendler, D., Kington, R., Madans, J., Wye, G. V., Christ-Schmidt, H., Pratt, L. A., Brawley, O. W., Gross, C. P. and Emanuel, E. (2005). Are Racial and Ethnic Minorities Less Willing to Participate in Health Research? *PLoS medicine* **3**(2): e19.

West, J. C., Marcus, S. C., Wilk, J., Countis, L. M., Regier, D. A. and Olfson, M. (2008). Use of depot antipsychotic medications for medication nonadherence in schizophrenia. *Schizophrenia bulletin* **34**(5): 995-1001.

Wheeler, A., Humberstone, V. and Robinson, E. (2008). Ethnic comparisons of antipsychotic use in schizophrenia. *Australian and New Zealand journal of psychiatry* **42**(10): 863-873.

Wheeler, A. J. (2008). Treatment pathway and patterns of clozapine prescribing for schizophrenia in New Zealand. *Annals of pharmacotherapy* **42**(6): 852-860.

Whiskey, E., Olofinjana, O. and Taylor, D. (2011). The importance of the recognition of benign ethnic neutropenia in black patients during treatment with clozapine: case reports and database study. *Journal of psychopharmacology* **25**(6): 842-845.

Williams, D. R., Gonzalez, H. M., Neighbors, H., Nesse, R., Abelson, J. M., Sweetman, J. and Jackson, J. S. (2007). Prevalence and distribution of major depressive disorder in African Americans, Caribbean blacks, and non-Hispanic whites: results from the National Survey of American Life. *Archives of general psychiatry* **64**(3): 305-315.

Wittkampf, L. C., Smeets, H. M., Knol, M. J., Geerlings, M. I., Braam, A. W. and De Wit, N. J. (2010). Differences in psychotropic drug prescriptions among ethnic groups in the Netherlands. *Social psychiatry and psychiatric epidemiology* **45**(8): 819-826.

Woods, S. W., Sullivan, M. C., Neuse, E. C., Diaz, E., Baker, C. B., Madonick, S. H., Griffith, E. E. and Steiner, J. L. (2003). Best practices: racial and ethnic effects on antipsychotic prescribing practices in a community mental health center. *Psychiatric services* **54**(2): 177-179.

World Health Organization (1985). *Targets for Health for All*.

Wyatt, R. J. (1991). Neuroleptics and the natural course of schizophrenia. *Schizophrenia bulletin* **17**(2): 325-351.

Wynn, G., Oesterheld, J., Cozza, K. and Armstrong, S. (2008). *Clinical Manual of Drug Interaction. Principles for Medical Practice*. Washington DC, American Psychiatric Publishing Inc.

Xiang, Y., Weng, Y., Leung, C., Tang, W. and Ungvari, G. (2006). Clinical and social determinants of use of depot antipsychotics for patients with schizophrenia in Hong Kong. *Hong Kong Journal of Psychiatry* **16**(2): 71.

Yang, J., He, M. M., Niu, W., Wrighton, S. A., Li, L., Liu, Y. and Li, C. (2012). Metabolic capabilities of cytochrome P450 enzymes in Chinese liver microsomes compared with those in Caucasian liver microsomes. *British journal of clinical pharmacology* **73**(2): 268-284.

Yang, M., Barner, J. C., Lawson, K. A., Rascati, K. L., Wilson, J. P., Crismon, M. L., Worchel, J. and Mascarenas, C. A. (2008). Antipsychotic medication utilization

trends among Texas veterans: 1997-2002. *Annals of pharmacotherapy* **42**(9): 1229-1238.

Yorston, G. and Pinney, A. (2000). Chlorpromazine equivalents and percentage of British National Formulary maximum recommended dose in patients receiving high-dose antipsychotics. *Psychiatric bulletin* **24**: 130-132.

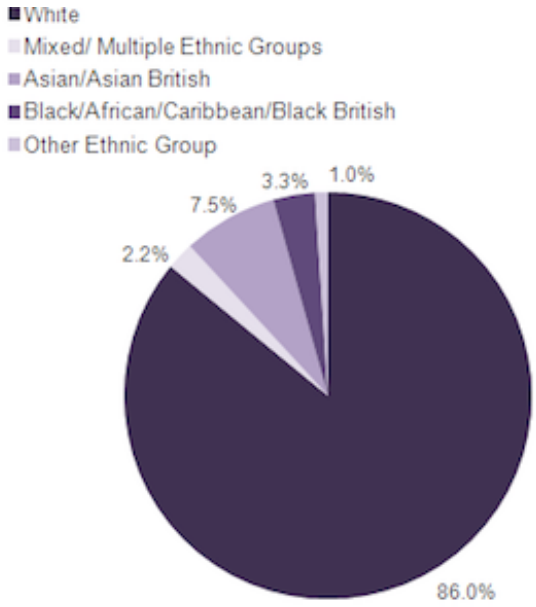
Zhou, S. F., Liu, J. P. and Chowbay, B. (2009). Polymorphism of human cytochrome P450 enzymes and its clinical impact. *Drug metabolism reviews* **41**(2): 89-295.

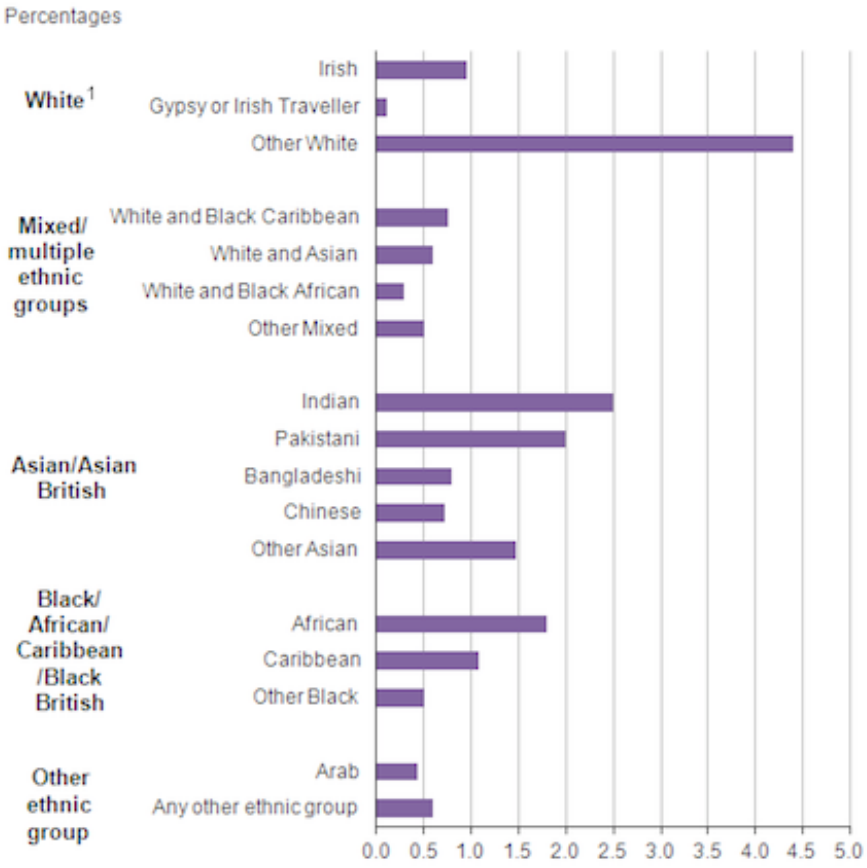
Zhou, X., Barber, W. H., Moore, C. K., Tee, L. Y., Aru, G., Harrison, S., Mangilog, B. and McDaniel, D. O. (2006). Frequency distribution of cytochrome P450 3A4 gene polymorphism in ethnic populations and in transplant recipients. *Research communications in molecular pathology and pharmacology* **119**(1-6): 89-104.

Zito, J. M., Safer, D. J., dosReis, S. and Riddle, M. A. (1998). Racial disparity in psychotropic medications prescribed for youths with Medicaid insurance in Maryland. *Journal of the American Academy of Child and Adolescent Psychiatry* **37**(2): 179-184.

APPENDICES

APPENDIX 1 ETHNIC GROUPS ENGLAND AND WALES 2011 CENSUS





APPENDIX 2 CONFOUNDERS COLLECTED BY OTHER STUDIES OF ANTIPSYCHOTICS AND ETHNICITY

Authors	Medication Outcomes	Confounders
(Dunn & Fahy, 1990)	Receipt of an antipsychotic.	No regression analysis. Chi-squared and t-tests by ethnicity and gender calculated.
(Flaskerud & Hu, 1992)	Treatment type.	Age, gender, ethnicity, diagnosis, primary language, socioeconomic status (income and dependents), therapists discipline (professional/non-professional), treatment modality (therapy with/without medication).
(Jann et al., 1992)	Plasma levels of haloperidol and metabolite by ethnicity; predictors of haloperidol concentrations.	Haloperidol dose, haloperidol metabolite levels, age by ethnicity, weight.
(Lloyd & Moodley, 1992)	Type and dose of antipsychotic medication.	Age, gender, ethnicity, diagnosis, section status.
(Lin et al., 1996)	Dose of antipsychotic	Age, gender, ethnicity, diagnosis, type, dose, other psychotropics.
(Segal et al., 1996)	Antipsychotic received; dose (in CPZe); number of doses; number of injections.	Ethnicity, psychotic diagnosis, GAS score (severity of psychiatric disturbance), dangerousness, psychiatric history, physical restraint used, hours spent in emergency service, clinicians efforts to engage patient in treatment.
(Delbello et al., 2000)	Use of antipsychotic treatment.	No regression just comparison of groups for age, gender, diagnosis, length of hospitalisation.
(Walkup et al., 2000)	Dose; factors predicting dose.	Ethnicity, length of stay, age, voluntary admission, weight, dangerousness, depression and substance misuse co-morbidity, BPRS (activation, withdrawal, depression/anxiety, paranoia subscales).
(Wang et al., 2000)	Predictors of antipsychotic medication treatment.	Age, education, marital status, race/ethnicity, psychiatric co-morbidity (Axis 1 conditions), psychiatrist visits in last 30 days.

Authors	Medication Outcomes	Confounders
(Baillargeon & Contreras, 2001)	Antipsychotic prescribing patterns in a prison setting.	Gender, age, race/ethnicity, violent offence status.
(Bayard-Burfield et al., 2001)	Risk of psychiatric illness; intake of psychiatric drugs.	Age, race/ethnicity, country of birth, language (knowledge and understanding), marital status, employment, psychiatric illness, taking psychotropic drugs, housing, migration because of political/religious instability or war, family or friends in Sweden, desire to leave Sweden, need for talking treatment but not sought, as many or more immigrants than Swedes in residential area.
(Owen, 2001)	Type of antipsychotic prescribed.	Centre, age, gender, ethnicity, marital status.
(Covell et al., 2002)	Type, route, polypharmacy.	Gender, age, race/ethnicity, marital status, education.
(Diaz & De Leon, 2002)	High dose antipsychotic treatment (> 1000mg CPZe).	Race/ethnicity, gender, smoking status, age, hospital centre (there were 2 in the study), long hospitalisation (>3 years), weight (> 90kg), depot antipsychotics, high potency antipsychotics, carbamazepine or phenytoin use.
(Emsley et al., 2002)	PANSS score changes with antipsychotics by ethnicity; response = 40% reduction in PANSS.	Age, gender, race/ethnicity.
(Fleck et al., 2002)	Antipsychotics prescribed; compliance.	Ethnicity, gender, weeks of follow-up, time in remission, time in psychosis during follow-up.
(Kuno & Rothbard, 2002)	Antipsychotic prescription patterns (type, route, treatment duration).	Age, gender, service type e.g. inpatient, emergency room, provider setting, social security receipt, ethnicity, depot treatment.
(Lelliott, 2002)	Antipsychotic polypharmacy.	Age, gender, bed type (forensic, rehabilitation, acute), polypharmacy, section status. diagnosis, ethnicity.
(Moore et al., 2002)	Psychotropic drug use.	No regression done.

Authors	Medication Outcomes	Confounders
(Copeland et al., 2003)	Type of antipsychotic prescribed.	Age, gender, substance misuse, diagnosis, race/ethnicity.
(Daumit et al., 2003)	Type of antipsychotic prescribed.	Age, gender, ethnicity, payment source (insurance/Medicare), geographic region, urban vs. rural practice location, physician practice setting, psychiatric diagnosis.
(Kreyenbuhl et al., 2003)	Dose, type, route, use of adjunctive or anticholinergic medicines.	Age, gender, ethnicity, education, state, diagnosis, medical co-morbidity.
(Leslie et al., 2003)	Use of psychotropic medication by ethnicity.	Age, gender, ethnicity, income, insurance type, known to psychiatric services, mood anxiety and attention deficit hyperactivity disorder comorbidity.
(Opolka et al., 2003)	Type of antipsychotic prescribed (specifically haloperidol or olanzapine).	Race/ethnicity gender, age, regional location, other mental illness, co-morbidities, prior antipsychotic use (previous clozapine use, previous depot use, previous SGA, number of previous antipsychotics in the last year), resources use (number of outpatient medical visits, emergency department visits, inpatient hospital days in last year).
(Pinninti et al., 2003)	Type of antipsychotic prescribed.	No regression.
(Szarek & Goethe, 2003)	Frequency of antipsychotic prescribing, type of antipsychotic.	Diagnosis, age, race/ethnicity, bipolar type, concurrent anxiety or substance misuse or any concurrent diagnosis.
(Taylor et al., 2003)	Number of antipsychotics prescribed before clozapine, theoretical time day in use of clozapine.	No regression only correlation coefficient and scatterplot. Looked at relationship between delay in clozapine use and gender, race/ethnicity, duration of illness separately.
(Woods et al., 2003)	Type of antipsychotic prescribed, route, polypharmacy.	Age, education, gender, race/ethnicity, diagnosis, substance misuse.

Authors	Medication Outcomes	Confounders
(Arnold et al., 2004)	Effect of gender/ethnicity interaction on antipsychotic dose, high dose, route, type, polypharmacy.	Age, ethnicity, education, income level, rating scale scores (HAM-D, GAF, YMRS, SAPS).
(Taylor, 2004)	Dose; co-prescription of clozapine and olanzapine with other antipsychotics.	No regression analysis only chi-squared tests done to compare co-prescription between paired ethnic groups. Demographics collected = age, race/ethnicity, gender.
(Van Dorn et al., 2005)	Effect of ethnicity and criminal arrest history on access to SGAs.	Gender, race/ethnicity, insurance, initial treatment setting, no visits with psychiatrist, GAF rating scale, history of substance misuse, history of violent behaviour, history of arrest, psychotic symptoms, compliance.
(Shi, 2007)	Patient characteristics and antipsychotic use patterns for oral and depot antipsychotics.	Age, gender, ethnicity, education, marital status, veteran status, insurance type, diagnosis, rating scales (PANSS, MADRAS, GAF), psychiatric hospitalisations in last year, arrest history, suicidal thoughts/attempts, substance misuse.
(Domino & Swartz, 2008)	Prevalence of antipsychotic prescribing; characteristics of antipsychotic users.	Age, gender, race/ethnicity, insurance status, family income, employment status, diagnosis.
(Grossman et al., 2008)	Functional genetic variation in drug metabolising enzymes and effect on dose, efficacy and safety of olanzapine, perphenazine, quetiapine, risperidone, ziprasidone.	Age, gender, race/ethnicity, weight, PANSS rating scale, smoking status, severe adverse effects, tardive dyskinesia status, antipsychotic use before study initiation, years since started treatment with antipsychotics, substance misuse, drug metabolising enzyme genotype status

Authors	Medication Outcomes	Confounders
(Wheeler et al., 2008)	Antipsychotic polypharmacy, type, route, dose, clozapine use at 2 time points (baseline time 1 in 2001 and time 2 in 2004).	Age, ethnicity and gender.
(Busch et al., 2009b)	Adherence to antipsychotic quality standards for receipt, continuity and dose.	Age, gender, substance misuse, diagnosis, race/ethnicity, fiscal year of treatment, region of residence.

APPENDIX 3 STUDIES OF ANTIPSYCHOTIC PRESCRIBING AND ETHNICITY

Authors	Number	Ethnicity	Type of study	Location	Medication Outcomes	Results	Comments
(Littlewood & Cross, 1980)	240	UK-born (white British), white immigrant, black immigrant	Survey	UK	Receipt of major tranquilliser (antipsychotic), depot antipsychotic use	Black patients were more likely than white to receive major tranquillisers (59% vs. 38%, $p<0.01$). Immigrant patients (black and white) were more likely than white British to receive intramuscular medication (71% vs. 49%, $p<0.025$).	Difference in major tranquilliser use not owing to diagnosis. Unusual ethnicity classification. Black-born British patient included in black immigrant group.
(Binder & Levy, 1981)	80	White, black, Asian (East)	Survey	USA	Dose	No significant difference in dose by ethnicity (values and statistics not listed, Asian vs. white or black).	Study examining EPSE, dose secondary outcome. Asians more likely to experience EPSE.
(Lin & Finder, 1983)	26	Asian/Asian American, white	Survey	USA	Dose (CPZe)	Asian patients treated with lower maximum ($p < 0.05$) and discharge ($p< 0.02$) doses than whites even after adjustment for body weight.	None
(Adams et al., 1984)	1311	Anglo (European), black, Hispanic	Survey	USA	Dose (CPZe), number of antipsychotics prescribed	No difference by ethnicity (ANOVA test) in oral or IM dosing of antipsychotics. Polypharmacy was less likely in Hispanics than other ethnic groups ($p<0.05$).	Does not state if polypharmacy less likely in Hispanics than blacks or Anglos or both these groups.
(Price et al., 1985)	397	White, black	Survey	USA	Predictors of use of depot fluphenazine decanoate vs. oral antipsychotics	Black patients were 2.2 times more likely than white to be receiving fluphenazine decanoate depot, $p< 0.001$ (controlled for gender and age).	None
(Holden, 1987)	100	White, black	Survey	South Africa	Dose	Dose for whites 381mg, blacks 92mg difference not tested statistically.	Study examining rates of tardive dyskinesia.
(Dunn & Fahy, 1990)	253	Black, White	Case note review	UK	Receipt of an antipsychotic	Black men were more likely to be given an antipsychotic than white men (90% vs. 63%, $p<0.001$).	No differences between black and white women.

Authors	Number	Ethnicity	Type of study	Location	Medication Outcomes	Results	Comments
(Chen et al., 1991)	66	Afro-Caribbean, non-Afro-Caribbean	Cohort	UK	Dose as CPZe (initial, cumulative, high dose), depot use	No difference in initial & cumulative dose by ethnicity. Afro-Caribbean patients more likely than non-Afro-Caribbean to be prescribed high doses (i.e. > 2000mg CPZe, $p<0.03$) and depots ($p<0.01$).	No significant difference in concurrent anticholinergic therapy.
(Flaskerud & Hu, 1992)	10599	Black, white, Asian, Latino	Survey	USA	Receipt of medication	Black patients more likely than whites to be prescribed medication in psychosis (OR 1.44 (95% CI 1.28, 1.61, $p<$ 0.00001).	None.
(Jann et al., 1992)	267 (Chinese 156, non-Chinese 111)	Black, Caucasian, Chinese, Hispanic	Pharmaco-kinetic study of haloperidol and metabolite concentrations.	Taiwan and USA	Dose of haloperidol	Hispanic patients were treated with higher doses than Caucasian and black ($p<0.05$). Black, Caucasian and Hispanic patients had higher doses than Chinese ($p=0.01$).	Small numbers of non-Chinese patients.
(Lloyd & Moodley, 1992)	138	Black, white	Survey	UK	Receipt, route, dose, polypharmacy	Black patients more likely than white to receive a depot and oral antipsychotic (40.5% vs. 20.8%, $p=0.019$) but not 2 oral antipsychotics. Black patients on a depot (but not oral) received higher median doses than white patients (180mg vs. 60mg CPZe, $p=0.04$). Black patients were as likely as white to receive an antipsychotic (OR 1.87, 95% CI 0.69, 5.82) or a depot (OR 1.49, 95% CI 0.94, 2.37).	None
(Tunnicliffe et al., 1992)	84	Afro-Caribbean, non-Afro-Caribbean	Survey	UK	Dose of depot antipsychotic	No significant difference in dose by ethnicity (no p value given).	None
(Stanley & Doyle, 1993)	5	White, black, mixed	Survey	UK	High dose (>1000mg CPZe)	No difference in high dose by ethnicity.	1 patient black, 1 mixed (black Asian)

Authors	Number	Ethnicity	Type of study	Location	Medication Outcomes	Results	Comments
(Strakowski et al., 1993)	173	Black, white	Survey	USA	Antipsychotic dose	Black patients received higher doses (haloperidol equivalents) than white (29.9mg vs. 15.3mg, p=0.001).	None
(Glazer et al., 1994)	398	White, non-white (97% black)	Prospective cohort	USA	Dose (CPZe), depot use	Non-white patients were more likely than white to have a higher dose of antipsychotic at baseline (p<0.001), a higher average dose during the study period (p<0.012) and a depot at baseline (p<0.001).	Study of risk factors for tardive dyskinesia. Non-white patients were almost all black (100/103 = 97%). Effect of ethnicity on dose was due to depot use.
(Chung et al., 1995)	164	African-American, white	Survey	USA	Dose, proportion on 'prn' neuroleptics	Mean daily dose (CPZe) was greater for African-Americans vs. white (389 mg and 280mg, p=0.05) Proportion of patients on 'prn' neuroleptics did not differ by ethnicity.	None
(Shubsachs et al., 1995)	124	Afro-Caribbean, non-Afro-Caribbean (Caucasian)	Survey	UK	Dose (CPZe)	Afro-Caribbean patients were more likely than Caucasians to be taking higher doses of antipsychotics at 4 weeks (882mg vs. 527mg, p<0.05) but not at 1 and 3 years after admission.	None
(Collazo et al., 1996)	72	Hispanic, Asian (Chinese), Anglo	Survey	USA	Mean maximum and stabilised, actual and standardised CPZE doses, anticholinergic medication use	Mean maximum actual and standardised CPZE doses; Hispanic (p<0.009) and Asian (p<0.002) lower than Anglo (no difference between Hispanic and Asian). Mean stabilised actual and standardised CPZE doses; Hispanic (p<0.036) but not Asian (p<0.056) lower than Anglo (no difference between Hispanic and Asian). No differences between groups on use of anticholinergic medication.	Follow-up study of Ruiz *et al,* 1996.
(Jeste et al., 1996)	66	Caucasian, African American	Observational study	USA	Dose (CPZe)	No difference in dose by ethnicity (t-test analysis).	None

Authors	Number	Ethnicity	Type of study	Location	Medication Outcomes	Results	Comments
(Lin et al., 1996)	403	Asian, non-Asian (Hispanic, African American and white)	Survey	USA	Dose of antipsychotic	Non-Asian ethnicity associated with higher doses of antipsychotics ($p<0.01$)	None
(Matsuda et al., 1996)	34 (data on 24)	Caucasian, Korean-American	Case control study	USA	Dose of clozapine	Korean-Americans were treated with lower daily doses of clozapine than Caucasians (366mg vs. 532mg, $p<0.025$). Plasma levels were also lower for Korean-Americans (212ng/L vs. 376ng/L, $p<0.05$)	Korean-Americans showed greater change in BPRS than Caucasians (48% vs. 37.1%, $p<0.05$).
(Ruiz et al., 1996)	103	Hispanic, Asian, General (non-Hispanic, non- Asian)	Survey	USA	Mean actual & weight standardised CPZe dose, anticholinergic medicines use	Hispanic and Asians had lower actual ($p<0.001$) and standard ($p<0.01$) CPZe doses than General ethnicity. No difference in dose between Hispanic and Asian. Asians prescribed anticholinergic medication more often than Hispanic or General ($p=0.0001$), Hispanic vs. General not reported.	General category poorly defined, 34 born outside of US.
(Segal et al., 1996)	442	African American, non-African American (Caucasian, Hispanic, Asian, other)	Observational study	USA	Antipsychotic received; dose (in CPZe); number of doses; number of injections, depot fluphenazine decanoate	African American patients were as likely to receive an antipsychotic (48% vs. 35%, OR 1.27 (no CI), $p=0.71$) as non-African Americans but a greater number of antipsychotic doses (3.1 vs.2.2, $p=0.02$); a higher 24-hour dose of antipsychotics (1321mg vs. 825mg, $p<0.001$); depot fluphenazine (8% vs. 2%, $p< 0.05$); and a greater number of antipsychotic injections ($p<0.04$).	Results were African Americans compared with non-African Americans.

Authors	Number	Ethnicity	Type of study	Location	Medication Outcomes	Results	Comments
(Lehman & Steinwachs, 1998)	719	White, African American, other	Database study	USA	Receipt of an antipsychotic, dose, high dose (> 1000mg CPZe), length of treatment, depot use, use of anticholinergic agents	No differences by race in receipt of an antipsychotic, dose, length of treatment and depot use. Minority patients more likely to be taking a high dose (27.4% vs. 15.9%, p=0.01) and to be taking prophylactic anticholinergic agents (64% vs. 40.3%, p= 0.003) than Caucasians when inpatients.	Analysed as white and Minority.
(Storch & Storch, 1998)	200	White, African American, Asian, Hispanic	Survey	USA	Prescribing of an antipsychotic	No significant difference African American and white (6% vs. 4.6%, p<0.05).	None
(Zito et al., 1998)	99,217	African American, Caucasian	Survey	USA	Psychotropic use in children aged 5-14 years	Caucasians (C) were twice as likely to be treated with an antipsychotic than African Americans (AA) (0.44% vs. 0.21%, ratio AA/C 1:2.1, no p value).	None
(Ruiz et al., 1999)	204	Black (African American), white, Hispanic	Survey	USA	Dose of antipsychotic	Mean dose in black and white patients was higher than in Hispanic patients (16.2mg, 15.5mg and 7.6mg respectively, no statistical test of difference). Similarly weight/dose ratios of black and white patients were higher than for Hispanics (p=0.0001 and p=0.001 respectively).	Doses converted to haloperidol equivalents. Patients on SGAs excluded.
(Delbello et al., 2000)	74	African American, Caucasian	Retrospective chart review	USA	Use of antipsychotic treatment.	African American patients were more likely than Caucasian to receive an antipsychotic (86% vs. 45%, p = 0.006).	Adolescents with bipolar disorder. Only14 African Americans in the study.
(Walkup et al., 2000)	293	African American, White	Survey	USA	High dose	African American patients more likely to be prescribed high doses (>1000mg CPZe) OR 2.67, p≤0.05 (no CI reported). This effect was *not significant* after controlling for depot use. Depot use increased risk of high dose by a factor of 30.	High doses in African American patients not explained by symptom severity at discharge.

Authors	Number	Ethnicity	Type of study	Location	Medication Outcomes	Results	Comments
(Wang et al., 2000)	154	Black, white, other	Survey	USA	Type (risperidone or olanzapine use vs. non-use)	White ethnicity associated with prescription of risperidone or olanzapine compared with other ethnicity (OR 0.11, 95% CI 0.02, 0.73) but not black (OR 0.46, 95% CI 0.13, 1.56)	None.
(Baillargeon & Contreras, 2001)	3750	Black, white, Hispanic	Survey	USA	Type of antipsychotic	Black (but not Hispanic) patients prescribed SGAs less frequently than white patients (OR 0.66, 95% CI 0.5, 0.87).	None.
(Leslie & Rosenheck, 2001)	34,925	Black, Hispanic, ?white (not listed))	Survey	USA	Antipsychotic polypharmacy, dose	Doses for black and Hispanic patients were not more or less than recommended. Black patients, but not Hispanic were less likely than ?white to be prescribed more than one antipsychotic (OR 0.833, 95% CI 0.748, 0.928).	Depot information not available for use in the study.
(Owen, 2001)	599	African American, Caucasian, Hispanic, Asian/Pacific Islanders	Survey	USA	Type of antipsychotic prescribed	Caucasian patients were more likely to receive SGAs than non-Caucasian patients (OR 0.509 (no 95% CI reported), $p \leq 0.001$).	None.
(Valenstein et al., 2001b)	1307 (234 on depot)	African-American, white, other (Asian, Hispanic, Native American)	Cohort study (baseline data analysis)	USA	Depot antipsychotic use by ethnicity; patient compliance by ethnicity; SGAs (post-hoc analysis)	African-American patients more likely to receive a depot antipsychotic than whites ($p=0.05$; regression analysis controlling for clinician rated-compliance black vs. white, OR 1.5, $p<0.05$, no CI quoted). Estimated compliance differed between 3 ethnicities ($p<0.05$). Black patients less likely to receive SGAs than whites ($p<0.001$).	Vs. other ethnicities not reported

Authors	Number	Ethnicity	Type of study	Location	Medication Outcomes	Results	Comments
(Valenstein et al., 2001a)	936	African-American, white, other (not stated)	Cross-sectional survey	USA	Dose – low (<300mg CPZe), recommended (300-1000mg CPZe), high (>1000mg CPZe)	African-American patients were more likely to receive high dose antipsychotics (39% vs. 25% (white) vs. 47% (other), $p<0.05$). Other ethnicity patients were more likely to receive low doses of antipsychotics (43% vs. 21% (white) vs. 13% (African American), $p<0.05$).	None
(Varner et al., 2001)	153	African American, Euro-American, Hispanic, Asian American	Retrospective cohort	USA	Dose	No difference by ethnicity in oral or depot dose ($p>0.05$).	None
(Covell et al., 2002)	386	African American, Caucasian, Latino/other	Survey	USA	Type, route, polypharmacy	Latino patients compared with non-Latino patients were less likely to be prescribed a SGA (OR 0.54, no CI, $p< 0.05$) and polypharmacy (OR 0.49, $p<0.05$), no data on depot use. Caucasian patients were more likely than non-Caucasian to receive a SGA (OR 1.75, $p<0.05$) and less likely to receive a depot (OR 0.47, $p<0.005$), no data on polypharmacy.	None.
(Diaz & De Leon, 2002)	595	African American, White	Survey	USA	High dose antipsychotic treatment (> 1000mg CPZe).	African American patients with schizophrenia high dose vs. white (not including high-potency antipsychotic variable) OR 1.55 (95% CI 1.02, 2.34, $p\leq0.05$).	High dose not associated with race in patients without schizophrenia & in total sample (except when high potency antipsychotics included).
(dosReis et al., 2002)	2714	African American, Caucasian	Cohort	USA	Dose in CPZe	African-Americans had a lower log dose vs. Caucasians (log -0.140, $p<0.01$)). African Americans on high potency antipsychotics had a higher log dose vs. Caucasians (log 0.269, $p<0.001$).	Three models described, race not a factor in two of the three.

Authors	Number	Ethnicity	Type of study	Location	Medication Outcomes	Results	Comments
(Fleck et al., 2002)	58	African American, white	Observational cohort of BPAD patients	USA	Length of treatment; type; compliance	African American patients were more likely to receive antipsychotics for a significantly greater period of follow-up ($p<0.007$) and FGA ($p<0.05$).	Poorer compliance for black patients compared with white ($p=0.01$). This did not explain differences in antipsychotic prescribing.
(Frackiewicz et al., 2002)	18	Hispanic, non-Hispanic	RCT	USA	Dose	No difference by ethnicity in baseline standardised (for weight) antipsychotic dose.	Pilot study, non-Hispanic group not homogenous, consisted of Indian, Filipino, 'American', Romanian, Jamaican and Pakistani patients.
(Kuno & Rothbard, 2002)	2515	Caucasian, African-American	Survey	USA	Type, route	Caucasian patients were significantly more likely than African-American to receive clozapine (OR 1.66, 95% CI 1.26, 2.18) and risperidone (OR 1.28, 95% CI 1.6, 1.55). African-Americans were more likely to receive depot antipsychotics ($p=0.001$) and a 'traditional' antipsychotic ($p=0.001$) than Caucasian patients.	White patients received mental health services more often and for longer, were more likely to have ICU management and less likely to have an emergency room contact than black patients.
(Lasser et al., 2002)	54,822 visits	White, black, Hispanic	Survey	USA	Visit rates (per 1000 population) for antipsychotic prescription	Black patients visited psychiatry or primary care providers for antipsychotic prescription fewer times than white (13.3 vs. 20.6, $p<0.05$). Hispanic no different to white.	Difference accounted for by psychiatry providers as analysis of primary care providers showed no difference by ethnicity in antipsychotic prescription per visit.
(Lelliott, 2002)	3576	Black, white, Asian, other	Survey	UK	Antipsychotic polypharmacy and high dose	No effect of ethnicity on either outcome.	None.
(Luo et al., 2002)	557	White, non-white	Database study	USA	Type of antipsychotic prescribed	White patients were more likely to receive a SGA than non-white (OR 2.335, 95% CI 1.271, 4.365, $p= 0.01$).	None

Authors	Number	Ethnicity	Type of study	Location	Medication Outcomes	Results	Comments
(Moore et al., 2002)	132	East Indian, African, mixed	Survey	Trinidad	Psychotropic drug use	No differences in prescribing of antipsychotic medication by ethnicity (p=0.390).	African and East Asian patients were prescribed SSRI-type antidepressants less often than mixed ethnicity patients (p=0.005).
(Copeland et al., 2003)	69,787	African American, white, Hispanic	Survey	USA	Type of antipsychotic prescribed, clozapine use	Hispanic (OR 0.77, 95% CI 0.73, 0.81) and African American (0.81, 95% CI 0.78, 0.84) patients less likely to receive a SGA than white. African American (OR 0.35, 95% CI 0.31, 0.39) and Hispanic (OR 0.33, CI 95% 0.26, 0.41) patients less likely to receive clozapine than white.	None
(Daumit et al., 2003)	5032	African American, white, Hispanic	Cross-sectional survey	USA	Type of antipsychotic prescribed	In 1992-1994, 1995-1997 and 1998-2000 African American patients were less likely than white patients to receive SGA for all diagnoses (1998-2000 OR 0.88, 95% CI 0.78, 0.97). In 1992-1994, 1995-1997 and 1998-2000 Hispanic patients had an equal chance of SGA use compared with white patients for all diagnoses (1998-2000 OR 1.05, 95% CI 0.92, 1.16).	None
(Jaffe & Levine, 2003)	2791	African American, white, Hispanic	Database study	USA	Antipsychotic polypharmacy	African American patients were more likely than white and Hispanic to receive antipsychotic polypharmacy (p<0.001).	None
(Kreyenbuhl et al., 2003)	344	African-American, Caucasian	Survey	USA	Dose, type, route, use of anticholinergic medicines	Black patients more likely to receive depot (OR 2.91, 95% CI 1.68, 5.01, p<0.0001); less likely to receive SGA (OR 0.24, 95% CI 0.12, 0.46, p=0.0001); more likely to receive anticholinergic medications (63% vs. 48%, p=0.008) compared with white patients. Doses did not differ by ethnicity.	Out-patient population.

Authors	Number	Ethnicity	Type of study	Location	Medication Outcomes	Results	Comments
(Mark et al., 2003)	2239	Black and non-black	Cohort study (baseline data analysis)	USA	Type of antipsychotic, depot use, anticholinergic use, adherence	Black patients less likely to be prescribed SGAs including clozapine ($p<0.05$). Black patients were more likely to be prescribed FGA (OR 1.64, 95% CI 1.27, 2.12, $p=0.0002$), anticholinergic agents ($p<0.05$), depots ($p<0.05$) and to be non-adherent ($p<0.05$).	Difference in FGA use by ethnicity remained even after controlling for depot use.
(Opolka et al., 2003)	2601	African American, white, Mexican American	Survey over 2 x 10 month time periods.	USA	Type of antipsychotic prescribed (specifically haloperidol or olanzapine)	African American patients less likely than white to receive olanzapine (OR 0.614, 95% CI 0.495, 0.761, $p<0.001$). Effect was consistent over 2 x 10 month periods. Mexican Americans less likely than white to receive olanzapine in 1st 10-month period (OR 0.607, no CI, $p=0.01$) but not in 2nd10-month period.	None.
(Owen et al., 2003)	130	African American, Caucasian	Survey	USA	Route (depot use), dose of antipsychotic (CPZe)	No difference by race/ethnicity in route of administration or dose after regression analysis.	CPZe used and analyses repeated for differing conversion factors.
(Pinninti et al., 2003)	164	Non-Caucasian (black + Asian), Caucasian	Cross-sectional Survey	USA	Type of antipsychotic prescribed	Non-Caucasian and Caucasian patients were as likely to be prescribed a SGA (86% vs. 68% respectively, no p value quoted, non-significant difference).	Outcome not adjusted for any variables.
(Szarek & Goethe, 2003)	535	Black, white, Hispanic	Survey	USA	Frequency of antipsychotic prescribing, type of antipsychotic	White patients (OR 0.289, 95% CI 0.157, 0.533) were less likely than black and Hispanic to be prescribed an antipsychotic. No difference in type of antipsychotic by ethnicity.	Patients with bipolar disorder.

Authors	Number	Ethnicity	Type of study	Location	Medication Outcomes	Results	Comments
(Valenti et al., 2003)	276	African Americans, Caucasians, other	Survey	USA	Predictors of conventional antipsychotic use	African Americans were more likely to be prescribed a conventional antipsychotic (OR 3.40, no CI, p<0.001) than Caucasians. African American and other patients were more likely to be taking conventional antipsychotics (OR 3.4, no CI, p<0.001).	None
(Taylor et al., 2003)	120	White, non-white (black, mixed, Asian)	Case note review	UK	Theoretical time delay in use of clozapine	Clozapine use not delayed by ethnicity (white 4.6 years vs. non-white 5.4 years, p=0.37).	None.
(Woods et al., 2003)	501	African American, non-African American (white, Hispanic, other)	Survey	USA	Type of antipsychotic prescribed, route, polypharmacy	African American patients were more likely to receive a depot than non-African American patients (OR 2.0, 95% CI 1.18, 3.41). No significant difference between African American and non-African American patients for receipt of a SGA (OR 0.725, 95% CI 0.48, 1.10) or polypharmacy (no statistics reported).	None.
(Arnold et al., 2004)	167	Black, white	Survey	USA	Effect of gender and ethnicity on antipsychotic high dose, route, type, polypharmacy	Black men more likely to be prescribed a depot antipsychotic than black women and white men and women (OR 2.6, 95% CI 1.19, 5.14, p<0.02). Black patients were more likely to be prescribed a high dose antipsychotic if they had a psychotic mood disorder (OR 8.1, 95% CI 1.15, 58.82, p<0.04).	No effect of ethnicity on high dose antipsychotic use in patients with schizophrenia, type of antipsychotic or polypharmacy. Controlled for age, education, income level, rating scale (illness severity).
(Bagchi et al., 2004)	350	White, African American, Latino	Survey	USA	Type of antipsychotic, receipt of an antipsychotic	Latinos (OR 0.20 95% CI 0.07, 0.56), but not African Americans, were less likely than white patients to receive a SGA. There was no difference by ethnicity in use of an antipsychotic.	Population were those with HIV and schizophrenia.

Authors	Number	Ethnicity	Type of study	Location	Medication Outcomes	Results	Comments
(Herbeck et al., 2004)	700	African American and white	Survey	USA	Type of antipsychotic	Black patients were less likely than whites to receive a SGA (OR 0.49, 95% CI 0.28, 0.85, p=0.011).	None
(Leslie & Rosenheck, 2004)	53,661	Black, Hispanic, (?white - not stated)	Survey	USA	Average daily dose, high dose	Black patients were more likely to receive both recommended doses (OR 1.09, no CI, p=0.003) and high doses (OR 1.28, no CI, p<0.0001) than ?white. Hispanic dose and high dose did not differ from ?white.	Depot information not available for use in the study.
(Opolka et al., 2004)	3583	African American, Mexican American, white	Survey	USA	Type of antipsychotic (olanzapine, risperidone or haloperidol)	African American patients but not Mexican American were less likely than white to receive olanzapine or risperidone compared to haloperidol (OR 0.66, 95% CI 0.54, 0.80, p<0.001). Ethnicity was not a predictor of risperidone vs. olanzapine use.	None
(Sohler et al., 2004)	501	Black, white	Cohort	USA	Dose (initial, discharge, maximum, average), route	No differences by ethnicity in dose and route in fully adjusted model.	Type of antipsychotic data collected but not analysed because of small numbers (SGA use black n=2, white n=23).
(Taylor, 2004)	475	Black, white, Asian	Survey	UK	Dose, polypharmacy of clozapine and olanzapine with other antipsychotics.	Black patients were more likely than white to be prescribed olanzapine with other antipsychotics (33% vs. 20%, p=0.023). No difference by ethnicity in dose of olanzapine and clozapine and polypharmacy with clozapine.	None.

Authors	Number	Ethnicity	Type of study	Location	Medication Outcomes	Results	Comments
(Ciliberto et al., 2005)	439	African American, Caucasian, other	RCT	USA	Efficacy (change in PANSS score), adverse effects (Extrapyramidal Symptom Rating Scale) and discontinuation rates of risperidone long-acting injection vs. placebo.	No difference by race/ethnicity in dose, efficacy, tolerability and discontinuation. No further details.	None.
(Opolka et al., 2004)	3583	African American, Mexican American, white	Survey	USA	Type of antipsychotic (olanzapine, risperidone or haloperidol)	African American patients but not Mexican American were less likely than white to receive olanzapine or risperidone compared with haloperidol (OR 0.66, 95% CI 0.54, 0.80, $p<0.001$). Ethnicity was not a predictor of risperidone vs. olanzapine use.	None
(Sohler et al., 2004)	501	Black, white	Cohort	USA	Dose (initial, discharge, maximum, average), route	No differences by ethnicity in dose and route in fully adjusted model.	Type of antipsychotic data collected but not analysed because of small numbers (SGA use black n=2, white n=23).
(Taylor, 2004)	475	Black, white, Asian	Survey	UK	Dose, polypharmacy of clozapine and olanzapine with other antipsychotics	Black patients were more likely than white to be prescribed olanzapine with other antipsychotics (33% vs. 20%, $p=0.023$). No difference by ethnicity in dose of olanzapine and clozapine and polypharmacy with clozapine.	None.

Authors	Number	Ethnicity	Type of study	Location	Medication Outcomes	Results	Comments
(Ciliberto et al., 2005)	439	African American, Caucasian, other	RCT	USA	Efficacy (change in PANSS score), adverse effects (Extrapyramidal Symptom Rating Scale), discontinuation rates of risperidone long-acting injection vs. placebo	No difference by race/ethnicity in dose, efficacy, tolerability and discontinuation. No further details.	None.
(Hudson et al., 2005)	2717	African American and white	Survey	USA	Type of antipsychotic FGA or SGA	Black patients were less likely to receive SGAs than white (OR 0.58, 95% CI 0.44, 0.75; p<0.001).	Nursing home residents.
(Kupfer et al., 2005)	2718	African American and Caucasian	Questionnaire	USA	Prescription of psychotropics for BPAD	African-Americans were more likely to be prescribed an antipsychotic than Caucasians (40.9% vs. 28.6%, p<0.001).	None
(Mace & Taylor, 2005)	1092	White, non-white	Survey	UK	Dose, high dose, co-prescription (FGA + SGA)	White patients were more likely than non-white to be prescribed a high dose antipsychotic (20.6% vs. 13.9%, p=0.02) but not percentage maximum dose (p=0.05) or co-prescription (p>0.05).	None
(Ng et al., 2005)	40	Asian, Caucasian	Survey	Australia and Singapore	Clozapine dose, plasma levels	Asian patients received a significantly lower mean dose of clozapine compared with Caucasians (175.6mg/day vs. 432.5mg/day, p<0.001) but levels similar. Dose by mg/kg also significantly lower for Asians (p<0.01).	Asian and Caucasian patients were not surveyed in the same country.

Authors	Number	Ethnicity	Type of study	Location	Medication Outcomes	Results	Comments
(Patel et al., 2005)	32	African American, Caucasian	Longitudinal survey	USA	Length of treatment with SGA, dose, receipt of an antipsychotic	African American adolescents received antipsychotics for a greater percentage of time than Caucasians (79% vs. 40%, p= 0.05). No difference by race/ethnicity in doses or receipt of an antipsychotic.	Adolescents with bipolar disorder. Hispanics excluded. Higher proportions of African American patients in this study diagnosed with psychotic features vs. Caucasian.
(Staller et al., 2005)	1292	White, non-white	Survey	USA	Prescription of an antipsychotic	No difference by ethnicity in being prescribed an antipsychotic (non-white vs. white OR 0.97, 95% CI 0.70, 1.34).	Child and adolescent population aged 1-18
(Van Dorn et al., 2005)	224	African American, white/other	Observational study	USA	Effect of ethnicity and criminal arrest history on access to SGAs	African American patients less likely than white/other to receive a SGA (OR 0.41, 95% CI 0.19, 0.89, p< 0.05). Both African American and white/other patients with a criminal arrest history were less likely to receive SGA than white/other without a history of arrest.	None
(Chakos et al., 2006)	1380	White, African American, other	RCT	USA	Predictors of baseline use of psychotropic medicines for schizophrenia in CATIE study	No significant difference between African American use of antipsychotics compared to white and other ethnicities.	African American patients were more likely not to be taking any psychotropic medication (OR 0.42, 95% CI 0.33, 0.54).
(Dickey et al., 2006)	329	White, black, other (American Indian, Asian American, Latino)	Observational study	USA	Dose, high dose (> 1000mg CPZe)	No difference in dose or high dose by ethnicity.	None
(Ferguson et al., 2006)	473	American Indian, European American	Retrospective chart review	USA	Use of psychotropic drugs	Antipsychotics were prescribed more often to European American children than American Indian (p<0.05) but after Bonferroni adjustment not significant (p=0.28).	African American and other ethnicities excluded because of low numbers in sample.

Authors	Number	Ethnicity	Type of study	Location	Medication Outcomes	Results	Comments
(Garver et al., 2006)	1113	Black, non-black	Retrospective cohort	USA	Prescription and type of antipsychotic in bipolar disorder	Black patients were more likely than non-black to receive a SGA ($p<0.001$). No differences by race/ethnicity in receipt of FGA or receipt of two or more SGAs.	More black than non-black patients received two or more psychotropics (12.6% vs. 8.5%, $p= 0.037$).
(Kelly et al., 2006)	373	African American and white	Survey	USA	Proportion of each ethnicity receiving clozapine, dose, time to clozapine discontinuation.	African Americans were treated with lower doses ($p=0.008$) and were less likely than whites to receive clozapine (10.3% vs. 15.3%, $p<0.001$). African Americans stopped clozapine during admission at a higher rate than whites ($p=0.041$).	White patients had higher total baseline BPRS scores than black patients at time of clozapine initiation ($p=0.005$). Black patients had greater improvement in BPRS scores initially than whites ($p=0.03$). Rates of hospital discharge did not differ between black and white patients
(Kilbourne & Pincus, 2006)	2958	Black, non-black	Survey	USA	Medication use in patients with BPAD	Black patients were more likely to receive a FGA than non-black (OR 1.42, 95% CI 1.04, 1.94) or any antipsychotic (OR 1.32, 95% CI 1.04, 1.67) and as likely to receive a SGA.	Adjusted for multiple confounders.
(Mallinger et al., 2006)	456	White and black	Cross-sectional Survey	USA	Treatment with SGA, clozapine use, combination of FGA and SGA	White patients were more likely to be treated with a SGA (OR 6.45, 95% CI 2.37, 17.54, $p< 0.001$), were more likely to be treated with clozapine (OR 2.70, 95% CI 1.58, 4.63, $p<0.001$) than black. Black patients were numerically more likely to receive a combination of a FGA and SGA (13% vs. 7%, no p value).	None
(Olfson et al., 2006)	1424	White non-Hispanic, other	Survey	USA	Receipt of an antipsychotic during physician visit	No difference by ethnicity in physician visits with or without antipsychotic treatment.	Population examined were youth < 20 years

Authors	Number	Ethnicity	Type of study	Location	Medication Outcomes	Results	Comments
(Valenstein et al., 2006)	104,082	Hispanic, black, white, other (Asian/Native American)	Survey	USA	Ziprasidone use and dose over 3 fiscal years	African American (OR ranged from 0.60 to 0.76; p<0.001) and Hispanic (OR ranged from 0.64-0.76; p range < 0.05, p<0.001) patients were less likely to receive ziprasidone than white patients over all 3 years. No difference between other and white.	None
(Connolly et al., 2007)	153	White, black	Cross-sectional Survey	UK	Dose, high dose, polypharmacy, type, cost	No differences in all outcomes by ethnicity except cost. Cost of treatment was higher in black patients compared with white (£182.79 vs. £143.08 p=0.02;OR > £150/month, 2.45, 95% CI 1.19, 5.08)	Single centre study.
(Gersing et al., 2007)	3268	African American, White	Database survey	USA	SGA use in children	African Americans were as likely as white patients to use a SGA (OR 1.34, 95% CI 0.98, 1.83).	None
(Kelly et al., 2007)	1875	African American and Caucasian	Cohort	USA	Discontinuation of clozapine.	No difference by ethnicity in proportions stopping clozapine overall. More black patients stopped because of leucopenia than whites (5.3% vs. 2.4%, p=0.001).	No black patients developed agranulocytosis.
(Kreyenbuhl et al., 2007b)	45,571	White, African-American, Hispanic, other	Retrospective database study	USA	Polypharmacy	African-American patients were less likely to be prescribed polypharmacy than whites (OR 0.81, 95% CI 0.75, 0.87). Hispanic and other ethnicities were as likely as whites to receive polypharmacy.	None
(Morrato et al., 2007)	55,481	White, black, Hispanic, Asian, other/unknown	Retrospective cohort	USA	Polypharmacy	Asian (not black or Hispanic) patients were more likely to be prescribed antipsychotic polypharmacy than white (OR 1.55, 95% CI 1.17, 2.04).	None
(Pogge et al., 2007)	309	White, black, Hispanic, other	Case-control study	USA	Receipt of SGA vs. no antipsychotic	No difference by ethnicity in use of SGA vs. no antipsychotic (p=0.08).	Adolescent population

Authors	Number	Ethnicity	Type of study	Location	Medication Outcomes	Results	Comments
(Shi, 2007)	2186	African American, white, other	Secondary analysis of 3- year naturalistic prospective study.	USA	Depot use	Black patients more likely to be treated with depot antipsychotics (OR 1.53, 95% CI 1.12, 2.09, p = 0.007) than 'other' ethnicity. White patients were less likely than 'other' ethnicity to be treated with depot than oral (OR 0.67, 95%CI 0.49, 0.92, p=0.012). White vs. black not compared.	Other predictors of greater use of depot than oral = PANSS disorganised thought, PANSS anxiety and depression, psychiatric hospitalisation in last year (yes), ever arrested (yes), current substance use (yes).
(Tamayo et al., 2007)	332	Latin American and white	RCT	USA, Mexico, Peru, Venezuela, Argentina, Brazil, Spain, France, Portugal, South Africa	Dose of olanzapine or haloperidol in acute mania	No significant difference between ethnicities in mean modal doses of both drugs.	Post-hoc analysis of RCT.
(Connolly & Taylor, 2008)	255	White and black	Cross-sectional Survey	UK	Dose, high dose, polypharmacy, type	No differences in all outcomes by ethnicity except polypharmacy (white 25.7% vs. black 31.1%, OR 3.05, 95% CI 1.44, 6.46, p=0.004).	Polypharmacy driven by centre differences, 1 of the 3 centres had very high rates of polypharmacy.
(Depp et al., 2008)	1473	Non-Latino white, Latino, African American	Database survey	USA	Use of mood stabiliser and/or antipsychotics in bipolar disorder	African Americans and Latinos were less likely to receive an antipsychotic alone than non-Latino whites ($p<0.001$ and $p = 0.011$ respectively).	None
(Domino & Swartz, 2008)	Not stated specifically (database of 23 000 - 35 000 subjects)	African American, white, Hispanic	Survey comparing data from 1996-7 to 2004-5.	USA	Prevalence of antipsychotic prescribing, characteristics of antipsychotic users.	No difference between ethnicities in probability of antipsychotic medication use (no values quoted).	None

Authors	Number	Ethnicity	Type of study	Location	Medication Outcomes	Results	Comments
(Grossman et al., 2008)	750	African American, white, other	Randomised Controlled Trial	USA	Functional genetic variation in drug metabolising enzymes (DME) and effect on dose, efficacy and safety of antipsychotics.	No effect of genetic variation in DME and dosing, efficacy and safety (including tardive dyskinesia) for olanzapine, perphenazine, quetiapine, risperidone, ziprasidone.	Analysis of CATIE study group.
(Jano et al., 2008)	621,719	White, Non-white	Survey	USA	SGA use	No difference in SGA use by ethnicity (white vs. non-white OR 1.14, 95% CI 0.54, 2.52, p=0.73)	Older adult (60 years and over) population
(Thorens et al., 2008)	92	Swiss, EU, non-EU	Questionnaire	Switzerland	Receipt of an antipsychotic	No difference by ethnicity in receipt of an antipsychotic p=0.26. No further details.	Patients defined by country of origin, Poland and Romania included in non-EU countries.
(West et al., 2008)	304	White, non-white	Questionnaire	USA	Depot initiation	Non-white (OR 1.14, 95% CI 0.53, 2.46) patients were as likely as white to receive a depot.	Non-white vs. white psychiatrists were more likely to initiate depots (27.6% vs. 13.1%, p=0.002)
(Yang et al., 2008)	8096	White, non-white (black, Hispanic, other (American Indian, native Hawaiian, Asian, Pacific Islander))	Survey	USA	Type of antipsychotic	Black (OR 0.754, 95% CI 0.622, 0.913) and Hispanic (OR 0.713, 95% CI 0.565, 0.899) patients (not other) less likely to use SGAs than white.	None

Authors	Number	Ethnicity	Type of study	Location	Medication Outcomes	Results	Comments
(Wheeler et al., 2008)	4821	European, New Zealand Maori, Pacific Islander, Asian	Survey	New Zealand	Antipsychotic polypharmacy, type, route, dose, clozapine use at 2 time points (baseline T1 in 2001 and T2 in 2004)	Antipsychotic monotherapy = numerical differences at T1 between ethnic groups but not at T2; type = SGA use increased, FGA use decreased, no differences between ethnicities at T2; route = depot use decreased - no differences between ethnicities at T2; clozapine = Asian patients lower use than other ethnicities; dose = significant difference between ethnicities at both T1 and T2 (lowest mean dose Asian, highest Maori).	Statistical differences between T1 and T2 measured, not between ethnic groups.
(Wheeler, 2008)	2796	European, New Zealand Maori, Pacific Nations, Asian, other	Survey	New Zealand	Clozapine use	Clozapine use differed by ethnicity (p=0.002).	None
(Ascher-Svanum et al., 2011)	931	White, African-American, other	Extension study (2 randomised controlled trials, 1 pharmacokinetic study)	International (more than 26 countries)	Predictors of olanzapine oral supplementation of olanzapine depot.	Being African-American was a predictor of increased use of oral supplementation with depot olanzapine (OR 1.85, 95% CI 1.004, 3.408, p = 0.049).	None
(Barnes et al., 2009)	1715	White, black, Asian, Chinese, mixed, other	Re-analysis of data from 3 audits	UK	Use of long-acting antipsychotic injections	No association between use of antipsychotic long-acting injections and ethnicity. No further information.	None
(Busch et al., 2009a)	13,497	Black, white, Hispanic, other	Observational study	USA	Filled prescription for an antipsychotic	No differences in use of antipsychotics for bipolar disorder for black (OR 0.93, 95% CI 0.87, 1.00) and Hispanic (OR 0.96, 95% CI 0.90, 1.03) compared with whites.	None.

Authors	Number	Ethnicity	Type of study	Location	Medication Outcomes	Results	Comments
(Busch et al., 2009b)	23,619	Black, white, Hispanic, other	Observational study	USA	Adherence to antipsychotic quality standards for receipt, continuity and dose (PORT standards)	Acute phase: medication prescribing (dose, continuous supply) worse for black vs. white (OR 0.86, 95% CI 0.79, 0.94), Hispanics same as whites. Maintenance phase: medication prescribing worse for black vs. white (OR 0.75, 95% CI 0.71, 0.79), Hispanics same as whites.	Acute phase: dose (PORT standards) similar for black vs. white; better for Hispanic vs. white patients (OR 1.69 (95% CI 1.04, 2.72). Maintenance phase: no difference in dose standard for black vs. white; better for Hispanic vs. white (OR 1.99 (95% CI 1.56, 2.55).
(Hanlon et al., 2009)	3480	Black, white	Longitudinal study	USA	Type, receipt of antipsychotic	Black patients were less likely to be prescribed SGA ($p=0.03$) than whites. Overall black patients were as likely as whites to be prescribed antipsychotics.	Older adults
(Hashmi et al., 2009)	178	Asian, white	Retrospective case-note review	UK	Switching from FGA to SGAs	Asian patients were as likely to be switched to SGAs as whites ($p=0.489$).	Minimal study details as published letter.
(Constantine et al., 2010b)	23,183	White, black, Hispanic, other	Database study	USA	Prevalence of antipsychotic polypharmacy	Other ethnicity more likely than white to receive antipsychotic polypharmacy (OR 1.18, 95% CI 1.04, 1.34, $p<0.001$).	Black and Hispanic as likely as white ethnicity to receive antipsychotic polypharmacy.
(Jin et al., 2010)	156	White, African American, Asian, mixed	Randomised Controlled Trial	USA	Effect of race/ethnicity and smoking on pharmacokinetics of perphenazine	Mean daily dose of perphenazine for African American patients did not differ from other ethnicities (25.04mg vs. 23.63mg, $p>0.05$)	Pharmacokinetic study of CATIE patients. African American mean clearance was significantly faster than non-black patients ($p<0.05$).

Authors	Number	Ethnicity	Type of study	Location	Medication Outcomes	Results	Comments
(Pinto et al., 2010)	1090	White, black/black British	Cross-sectional Survey	UK	Prescription, type, route of antipsychotic	Black patients were more likely to be prescribed a depot antipsychotic than white patients (OR 2.06, 95% CI 1.18, 3.59, p=0.011), and more likely to be prescribed a depot as the only antipsychotic ever taken (OR 2.71, 95% CI 1.13, 6.53, p=0.026). No difference by ethnicity in type or prescription of an antipsychotic.	None
(Ponto et al., 2010)	371	Malay, Chinese, Indian	Cross-sectional Survey	Malaysia	Dose (CPZe)	No differences in dose by ethnicity (actual values not stated).	None
(Sleath et al., 2010)	64,775	White, black, Unknown	Database study	USA	Receipt of an antipsychotic	Black patients were as likely and Unknown race/ethnicity (p<0.001) more likely than white to receive an antipsychotic.	Sample were youth under 18, multiple regression analysis conducted.
(Stevenson et al., 2010)	12.090	White, non-white	Cross-sectional survey	USA	Antipsychotic use and indication	No difference in antipsychotic use for white vs. non-white (reference) patients (OR 1.14, 95% CI 0.9, 1.46, p=0.27). No difference by ethnicity in appropriate (p=0.16), potentially appropriate (p=1.0) and no appropriate indication (p=0.65) for antipsychotics.	Nursing home residents aged 60 and over.
(Wittkampf et al., 2010)	852,213	Moroccan, Turkish, Native (Dutch and Western)	Survey	The Netherlands	Use of psychotropics by ethnicity	Moroccan (OR 1.15, 95% CI 1.10, 1.21) and Turkish (OR 1.12, 95% CI 1.05, 1.18) patients were more likely than Native to be prescribed an antipsychotic.	None
(Connolly et al., 2011)	938	White and black	Cross-sectional Survey	UK	Dose, high dose, polypharmacy, type, cost	No differences in all adjusted outcomes by ethnicity.	8 centre study.
(Degenhardt et al., 2011)	231	African American and Caucasian	Pooled randomised controlled trials	USA	Mean modal dose	No differences by ethnicity for dose.	Small number of African American patients in the study (n=41).

Authors	Number	Ethnicity	Type of study	Location	Medication Outcomes	Results	Comments
(Douzenis et al., 2011)	153	Greek, non-Greek	Observational study	Greece	Treatment outcome (GAF, BPRS), polypharmacy, type of antipsychotic	No significant differences for treatment outcome, polypharmacy and type of antipsychotic (chi-squared and Mann Whitney).	Most of immigrant group were Albanian (32 of 63).
(el-Badri & Mellsop, 2011)	201	Maori, European, other	Database study	New Zealand	Dose, length of treatment on clozapine	No differences in these outcomes by ethnicity. No individual ethnic group comparisons.	None
(Findling et al., 2011)	157	White, other	Cohort study secondary analysis	USA	Receipt of antipsychotics in children with mania	White patients were more likely to be prescribed an antipsychotic than other ethnicity (OR 2.32, 95% CI 1.37, 3.91).	Ethnicity defined as white or other ethnicity only
(Puyat et al., 2011)	27,658	White, Chinese, other Asian, Non-white/Non Asian, mixed	Cross-sectional Survey	Canada	Prescription of an antipsychotic	Chinese patients (OR 0.49, 95% CI 0.25, 0.98, $p<0.05$) were less likely and mixed patients (OR 2.97, 95% CI 1.30, 6.80) were more likely than white to be using antipsychotic medication. Other Asian and non-white/Non-Asian did not differ from white.	Non-white included black patients.
(Rost et al., 2011)	3359	Non-Hispanic white, Hispanic, non-Hispanic black, other	Survey	USA	Management of antipsychotic medication	Non-Hispanic blacks were more likely to have management of antipsychotic medication than non-Hispanic whites in 3 of the 4 regression models (OR range 1.66 to 1.88, $p<05$). Hispanic and other ethnicity did not differ from whites.	Outcome defined as medications prescribed, ordered, supplied, administered or continued. Non-Hispanic blacks had greater risks of hospitalisation in all 4 models.
(Aggarwal et al., 2012a)*	102	Black, white, Hispanic, other	Survey	USA	Use and type of antipsychotic long-acting IM injections	White less likely than non-white to use long-acting injections (OR 0.52, 95% CI 0.33, 8.3, $p<0.007$). Race/ethnicity not associated with type of injectable antipsychotics (1^{st} or 2^{nd} generation).	CI for odds ratio cross 1 but p value highly significant.

Authors	Number	Ethnicity	Type of study	Location	Medication Outcomes	Results	Comments
(Aggarwal et al., 2012b)*	124	Black, white, Hispanic + mixed, other	Survey	USA	Antipsychotic polypharmacy (oral treatment in those on long-acting IM injections)	Greater use of oral antipsychotics with depot in Hispanic patients (OR 3.8, 95% CI 1.3-10.8). Other comparisons not quoted.	Reference category for logistic regression not listed. Author contacted no reply. Hispanics grouped with mixed incorrectly.
(Coury et al., 2012)	2853	Caucasian, non-Caucasian, Hispanic/Latino, non-Hispanic/Latino	Database study	USA	Rates of psychotropic use in children and adolescents	Hispanic/Latino patients were less likely to receive a SGA than non-Hispanic/Latino patients ($p<0.03$). Caucasian vs. non-Caucasian not significantly different.	None
(Cruz et al., 2012)	206,603	Native-born, immigrants (Eastern Europe, Maghreb (North Africa), Latin America, Sub-Sahara Africa, other)	Cross-sectional survey	Spain	Proportions of each group treated with antipsychotics, type of antipsychotic prescribed	Native-born were numerically more likely to be treated with antipsychotic than immigrants (1.9% vs. 0.4%). No observed differences for type of antipsychotic.	No statistical analysis of between group differences for exposure to antipsychotic medication or type.
(Fastenau et al., 2012)	217	Caucasian, other ethnicities not stated in abstract	Database study	USA	Long-acting injection use	Ethnicity not a factor after regression analysis however before adjustment Caucasians were less likely than other races/ethnicities to receive a long-acting injection (47.9% vs. 55.4%, $p=0.03$).	Abstract only available so no details of ethnic groups.
(Horvitz-Lennon et al., 2012)	13,992	Black, Latino, white	Cohort study	USA	Use of RLAI	Black (OR 1.09, 95% CI 0.89, 1.33) and Latino (OR 0.90, 95% CI 0.72, 1.12) patients were not less likely than white to use RLAI.	None
(Howes et al., 2012)	149	White, black, Asian, mixed other	Retrospective cohort study	UK	Theoretical delay in time to prescription of clozapine	No difference by ethnicity in delay in time to prescribe clozapine (white mean 48.3 months; other mean 47.4 months; $p=0.9$).	Ethnicity (black, Asian and mixed) was a significant factor in patients excluded from the study because of missing data.

Authors	Number	Ethnicity	Type of study	Location	Medication Outcomes	Results	Comments
(Koranek et al., 2012)	1807	Caucasian, African American, Hispanic, other	Retrospective chart review	USA	Prescribing of FGA and SGAs after CATIE study.	African-American patients were more likely than Caucasians to be prescribed a FGA (OR 2.36, 95% CI 1.61, 3.48) but not Hispanic or other ethnicities.	None
(Koranek et al., 2012)	1807	Caucasian, African American, Hispanic, other	Retrospective chart review	USA	Prescribing of FGA and SGAs after CATIE study.	African-American patients were more likely than Caucasians to be prescribed a FGA (OR 2.36, 95% CI 1.61, 3.48) but not Hispanic or other ethnicities.	None
(Leslie & Rosenheck, 2012)	214,113	White, black, Hispanic, other	Cohort study	USA	Use of 'off-label' antipsychotic medications	Black (OR 0.90, 95% CI 0.88, 0.91) and Hispanic (OR 0.80, 95% CI 0.79, 0.82) patients were less likely than white to be prescribed any 'off-label' antipsychotics. other ethnicity did not differ from white.	'Off-label' was defined as not having BPAD or schizophrenia.
(Manuel et al., 2012)	144	Black, white, Hispanic, other	Survey	USA	Factors associated with starting clozapine	Black (OR 0.57, 95% CI 0.38, 0.86) and Hispanic (OR 0.47, 95% CI 0.24, 0.91) patients were less likely than whites to start clozapine. Other not reported in regression analysis.	None
(Nejtek et al., 2012)	54	African American and white	Cross-sectional survey	USA	Antipsychotic dose (mean CPZe)	African American men received similar doses of antipsychotic as white men (p=0.257). Doses for black women were also similar to white women (p = 0.921). White men received higher doses than African American women (p=0.034).	None

Authors	Number	Ethnicity	Type of study	Location	Medication Outcomes	Results	Comments
(Robst, 2012)	12810 (use and cost), 6393 (dose)	Black, white, Hispanic, other	Mirror image study	USA	Use of an antipsychotic, dose, polypharmacy, cost	Use of an antipsychotic was lower for blacks (OR 0.84, 95% CI 0.75, 0.93) and higher for Hispanics (OR 1.54, 95% CI 1.42, 1.68) and other (OR 1.34, 95% CI 1.20, 1.50) than whites. Black (OR 0.77, 95% CI 0.65, 0.91), Hispanic (OR 0.71, 95% CI 0.63, 0.80) and other (OR 0.81, 95% CI 0.68, 0.96) had a higher risk of non-recommended doses than whites. Rates of polypharmacy were not significantly different between black Hispanic and others vs. white. Costs were lower for black (-1.183, $p<0.001$), greater for Hispanic (1.436, $p<0.001$) and other (0.890, $p<0.001$) than whites.	Use, cost, dose pre and post introduction of Medicaid prepaid health plans.
(Dusetzina et al., 2013)	7901	White, black, Hispanic	Cross-sectional survey	USA	Use of olanzapine pre and post FDA metabolic effect warnings	Hispanic patients had a greater use of olanzapine than white both pre (risk difference 0.17, 95% CI 0.13, 0.20) and post (risk difference 0.03, 95% CI 0.1, 0.4) FDA warning. There was no difference for black vs. white use pre and post warning.	Excluded Asian and other ethnic groups.
(Arnold et al., 2013)	722	Non-Hispanic whites, African-Americans, Hispanics	Randomised trial	USA	Dose of antipsychotic	Prescribed daily dose differed by ethnicity (which not stated) for risperidone only (not other antipsychotics) ($p=0.04$). Non-Hispanic whites had the highest average dose (4.4mg) followed by African Americans (4mg) then Hispanics (3.9mg).	Data from CATIE (Clinical Antipsychotic Trials of Intervention Effectiveness).
(Hassan et al., 2013)	209	White European, non-white European	Survey	Canada	Chlorpromazine equivalent (CPZe) dose by ethnicity	No difference by ethnicity (white CPZe dose 515.72mg vs. non-white 516.08, $p=0.972$).	Ethnicity was both self-reported and genetically tested.

Authors	Number	Ethnicity	Type of study	Location	Medication Outcomes	Results	Comments
(Horvitz-Lennon et al., 2013)	20,122	Black, Latino, non-Latino white	Survey	USA	Clozapine use	Proportions of blacks (2.3%) and Latinos (2.1%) using clozapine were lower than non-Latino whites (5.9%).	Differences not tested statistically. *My analysis* (chi-squared) $p<0.01$ Black vs. white also for Latino vs. white.
(Linares et al., 2013)	252	Black (African American/African descent), Latino, mixed/other (Asian, white)	Prospective cohort	USA	SGA use in children	Black patients more likely than Latino (OR 5.10, 95% CI 1.15, 9.19, $p<0.001$) and mixed/other (OR 3.26, 95% CI 1.9, 13.67, $p<0.05$) to be prescribed SGAs.	In mixed group 69% were Latino and black.
(Metcalfe et al., 2013)	31,889,448 prescriptions	Maori, non-Maori	Survey	New Zealand	Prescriptions dispensed for antipsychotics	Greater number of excess prescriptions dispensed for depot older antipsychotics and a shortfall in prescriptions for oral newer antipsychotics for Maori vs. non-Maori.	Study examined prescriptions dispensed linked with disease burden for each ethnicity.
(Puyat et al., 2013)	12 studies	African American, Latino, Asian, Maori, Pacific Islanders, black British	Systematic review and meta-analysis	International	Use of an antipsychotic, type of antipsychotic	No significant differences in odds of using antipsychotics for African Americans vs. non-African Americans; Latinos vs. non-Latinos; Asians, Maoris and Pacific Islanders vs. non ethnic minority; black/black British vs. white. African Americans (OR 0.62, 95% CI 0.50, 0.78) vs. non-African Americans and Latinos (OR 0.77, 95% CI 0.73, 0.81) vs. non-Latinos were less likely to receive newer antipsychotics.	Included studies with outpatients and OR quoted, did not include some key studies.

Authors	Number	Ethnicity	Type of study	Location	Medication Outcomes	Results	Comments
(Teo et al., 2013)	497	White European and non-white European	Survey	Canada	Treatment resistance and ethnicity, antipsychotic polypharmacy, clozapine use	Polypharmacy more likely in white patients than non-white (p=0.05). Clozapine use (p=0.979) and clozapine use in polypharmacy (p=0.502) did not differ by ethnicity.	Treatment resistance more likely in white patients than non-white (p=0.031).
(Brown et al., 2014)	102,884	African-Americans, Caucasians, other	Survey	USA	Receipt of depot antipsychotic by race/ethnicity	African-Americans were numerically more likely to receive depot antipsychotics than Caucasian and other ethnicities (quoted by individual US state).	Descriptive statistics only no significance testing.
(Rodday et al., 2014)	340	White/non-Hispanic, other	Survey	USA	'Off label' use of antipsychotics	White/non-Hispanics (OR 0.28, 95% CI 0.16, 0.51) were less likely to use 'off label' SGAs than other.	Survey of child and adolescents psychiatrists.
(Stroup et al., 2014)	629,809 treatment episodes	White/non-Hispanic, African American/non-Hispanic, Hispanic, other	Survey	USA	Factors associated with clozapine initiation	African Americans (OR 0.663, 95% CI 0.61, 0.72), Hispanic (OR 0.788, 95% CI 0.71, 0.87) and other ethnicities (OR 0.889, 95% CI 0.84, 0.94) were less likely to start clozapine compared with whites.	None
(Cataife & Weinberg, 2015)	5,843,711	White, African-American, American Indian /Alaska Native, Asian, Hispanic, Hawaiian or multiracial, Unknown	Survey	USA	Antipsychotic use	White patients had a shorter time to antipsychotic prescription ($p<0.001$ for all except Hawaiian/multiracial $p<0.05$) and also had a higher antipsychotic fill probability than all other ethnicities ($p<0.01$).	Children and adolescents (ages 2 to 20).

Authors	Number	Ethnicity	Type of study	Location	Medication Outcomes	Results	Comments
(Kamble et al., 2015)	61,793	White, black, other	Retrospective cohort	USA	Factors associated with co-prescription of stimulant with SGA	Black patients were more likely than white to be prescribed concurrent stimulants and SGA (OR 1.34, 95% CI 1.26, 1.41) but not other ethnicity (OR 1.00,95% CI 0.94, 1.05).	Concurrent use of stimulants and SGA in children (aged 6 to 17) with ADHD.
(Lawson et al., 2015)	15,123	White, black	Retrospective cohort	USA	Antipsychotic use, type, route	No difference between black and white patients antipsychotic use (OR 1.0, 95% CI 0.90, 1.12, p=0.952). In 2012 black patients (reference category) were less likely than white to receive oral SGA (OR 1.43, 95% CI 1.32, 1.56, p<0.001) and more likely to receive oral FGA (OR 0.87, 95% CI 0.79, 0.96, p=0.003), LAI FGA (OR 0.47, 95% CI 0.42, 0.53, p<0.001) and LAI SGA (OR 0.83, 95% CI 0.74, 0.93, p=0.001).	Medicaid database
(McCutcheon et al., 2015)	36	White British, black, other	Survey	UK	Antipsychotic plasma levels	Black patients were more likely to have low antipsychotic plasma levels than white/other ethnicity patients (p=0.02).	None
(Velligan et al., 2015)	2919	White, non-white (black, other)	Survey	USA	Outcomes of clozapine use vs. antipsychotic polypharmacy	Fewer white vs. non-white patients in clozapine monotherapy group vs. polypharmacy group (52% vs. 61%, no p value). Polypharmacy group differs by race/ethnicity (not specified which) from clozapine group (p<0.001).	None
(Burgio et al., 2016)	4891	African-American, white	Survey	USA	Antipsychotic use and administration in end of life care	African Americans were less likely than whites to have an antipsychotic administered (OR 0.73, 95% CI 0.62,0.86, p= 0.004) but not an antipsychotic ordered (OR 0.87, 95% CI 0.73,1.04, p= 0.138).	None

Authors	Number	Ethnicity	Type of study	Location	Medication Outcomes	Results	Comments
(Dey et al., 2016)	451	Maori, non-Maori =New Zealand European, Asian, Pacific Islander and other	Survey	New Zealand	Antipsychotic dose (CPZe), clozapine use	No differences in dose by ethnicity (p=0.09) but Maori were prescribed clozapine more frequently than non-Maori (24% vs. 13%, p=0.007). No difference by ethnicity in type or route of antipsychotic.	None
(Herzig et al., 2016)	17,775	White, black, Asian, Hispanic, other	Retrospective cohort	USA	In-hospital exposure to and discharge on an antipsychotic	Black patients were less likely than white to receive an antipsychotic RR 0.8 (95% CI 0.6, 0.96).	Scope of use of antipsychotics for delirium. Small sample size for Asian, Hispanic and other ethnic groups.
(Cook et al., 2017)	22,524	Non-Latino white, non-Latino black, Latino	Survey	USA	Antipsychotic use	White patients (with and without psychological impairment) were more likely to be prescribed SGA than black and Latino (1.2% vs. 0.8% vs. 0.6%, p<0.05).	Children and adolescents aged 5 to 17
(Moore & Mattison, 2017)	40.4 million	White/other, black, Asian, Hispanic	Survey	USA	Psychotropic use (including antipsychotics)	Antipsychotics used for white 1.7%, black 1.9%, Asian 0.7% and Hispanic 1.3%. White patients used psychotropics more frequently than Hispanic (OR 3.1, 95% CI 2.7, 3.5) but not Asian (vs. Hispanic) or black (vs. Hispanic).	Sample size for all psychotropics. Numerical analysis only for antipsychotics.

Authors	Number	Ethnicity	Type of study	Location	Medication Outcomes	Results	Comments
(Tang et al., 2017)	650	Hispanic, non-Hispanic black	Cohort study	USA	Clozapine use, antipsychotic polypharmacy (≥90 days, non-clozapine combinations)	Prescribers with higher percentages of ethnic minority patients were less likely to prescribe clozapine and polypharmacy than those with lower percentages. Hispanic patients clozapine use (OR 0.97, 95% CI 0.96, 0.98, p=0.001), polypharmacy use (OR 0.99, 95% CI 0.98, 0.99, p<0.001). Non-Hispanic black clozapine (OR 0.99, 95% CI 0.99. 0.99,p<0.001) polypharmacy (OR 1.00, 95% CI 0.99,1.00, p<0.05).	Compared prescribing for prescribers with high and low proportions of ethnic minorities not vs. another ethnic group.
(Das-Munshi et al., 2018)	10,512	White, Black, Asian, Chinese/Other, Mixed	Cross-sectional survey	UK	Antipsychotic receipt, type (FGA or SGA), depot use, clozapine use, high dose, prescribed 2+ antipsychotics (excluding clozapine), involvement of service-user in antipsychotic choice, provided with written information on antipsychotic, benefits/side effects of antipsychotic explained	Depot use was more likely in black patients than white (OR 1.56, 95% CI 1.33, 1.84). Clozapine use less likely in black vs. white patients (OR 0.56, 95% CI 0.39, 0.79. High dose antipsychotic use more likely in mixed vs. white patients (OR 1.58, 95% CI 1.05, 2.38). No differences between ethnic groups and white patients for other outcomes.	Multicentre study, community patients. Multi-level multivariable logistic regression models. Adjusted for 7 confounders including ethnicity.

* same dataset; ADHD = attention deficit hyperactivity disorder; B= black; BPAD = bipolar affective disorder; BPRS = Brief Psychiatric Rating Scale; CATIE = Clinical Antipsychotic Trials for Intervention Effectiveness; CGI-S = Clinical Global Impression – Severity; CI = confidence interval; CPZe = chlorpromazine equivalents; EPSE = extrapyramidal side effects; GAF = Global Assessment of Functioning; IM = intramuscular; LAI = long-acting injection; PANSS = Positive and Negative Syndrome Scale; PORT = Patient Outcomes Research Team; RCT = randomised controlled trial; RR = risk ratio; RLAI = risperidone long-acting injection; SUD = substance misuse disorder; UK = United Kingdom; United States of America = USA.

APPENDIX 4 STUDIES OF ANTIPSYCHOTIC PRESCRIBING AND ETHNICITY, SUMMARY TABLE

Notes

- Worse = greater receipt of/length of treatment of an antipsychotic; greater depot use; lesser use of clozapine; lesser use of SGAs; greater FGA use; greater use of 'off label' antipsychotics; more than one antipsychotic concurrently; lower cost
- Some references appear in more than one grouping because of multiple ethnic comparisons

Black vs. white (reference category)

Reference	Outcome	Worse	No Difference	Better	Comments
(Littlewood & Cross, 1980)	Antipsychotic use	■			None
	Depot use	■			
(Adams et al., 1984)	Dose		■		None
	Polypharmacy		■		
(Price et al., 1985)	Depot use	■			None
(Holden, 1987)	Dose			■	None
(Dunn & Fahy, 1990)	Antipsychotic use	■			None
(Chen et al., 1991)	Dose		■		Non-Caribbean assumed white
	Depot use	■			
	High dose	■			
(Flaskerud & Hu, 1992)	Antipsychotic use	■			Medication receipt in psychosis

Reference	Outcome	Worse	No Difference	Better	Comments
(Lloyd & Moodley, 1992)	Depot use		■		None
	Antipsychotic use		■		
	Polypharmacy - depot and oral	■			
	Depot dose	■			
	Oral dose		■		
	Polypharmacy -2 oral		■		
(Stanley & Doyle, 1993)	High dose		■		Included 1 patient of mixed race
(Strakowski et al., 1993)	Dose	■			None
(Glazer et al., 1994)	Dose	■			None
	Depot use	■			
(Chung et al., 1995)	Dose	■			None
	PRN antipsychotics		■		
(Shubsachs et al., 1995)	Dose 4 weeks after admission	■			None
	Dose 1 year and 3 years after admission		■		
(Jeste et al., 1996)	Dose		■		None
(Storch & Storch, 1998)	Antipsychotic use		■		None
(Zito et al., 1998)	Antipsychotic use	■			None
(Delbello et al., 2000)	Antipsychotic use	■			None
(Walkup et al., 2000)	High dose		■		None
(Wang et al., 2000)	Type of antipsychotic (2^{nd} generation)		■		None

Reference	Outcome	Worse	No Difference	Better	Comments
(Baillargeon & Contreras, 2001)	Type of antipsychotic (2nd generation)	■			None
(Leslie & Rosenheck, 2001)	Dose		■		None
	Polypharmacy			■	
(Valenstein et al., 2001a)	High dose	■			None
(Valenstein et al., 2001b)	Depot use				None
	Type of antipsychotic (2nd generation)				
(Diaz & De Leon, 2002)	High dose				In patients with schizophrenia
(dosReis et al., 2002)	Dose – low and high potency antipsychotic			■	None
	Dose - high potency antipsychotic	■			
(Fleck et al., 2002)	Length of treatment				None
	Type (1st generation)				
(Kuno & Rothbard, 2002)	Type (2nd generations)				None
	Clozapine use				
	Depot use				
(Lasser et al., 2002)	Antipsychotic use				Visit rates for antipsychotic prescription
(Copeland et al., 2003)	Type (2nd generation)				None
	Clozapine use				
(Daumit et al., 2003)	Type (2nd generation)				None

Reference	Outcome	Worse	No Difference	Better	Comments
(Jaffe & Levine, 2003)	Polypharmacy	■			None
(Kreyenbuhl et al., 2003)	Dose		■		None
	Type (2nd generation)	■			
	Depot use				
	Anticholinergic agent use				
(Opolka et al., 2003)	Type (2nd generation)				None
(Owen et al., 2003)	Dose		■		None
	Depot use				
(Valenti et al., 2003)	Type (1st generation)	■			None
(Arnold et al., 2004)	High dose		■		Depot use worse for black men not black women
	Depot use	■			
	Type (2nd generation)		■		
	Polypharmacy				
(Bagchi et al., 2004)	Type (2nd generation)				None
	Antipsychotic use				
(Herbeck et al., 2004)	Type (2nd generation)	■			None
(Leslie & Rosenheck, 2004)	Dose			■	None
	High dose	■			
(Opolka et al., 2004)	Type (2nd generation)				None
(Sohler et al., 2004)	Dose		■		None
	Route				

Reference	Outcome	Worse	No Difference	Better	Comments
(Taylor, 2004)	Dose		■		None
	Polypharmacy (with clozapine)		■		
	Polypharmacy (with olanzapine)	■			
(Hudson et al., 2005)	Type (2nd generation)	■			None
(Kupfer et al., 2005)	Antipsychotic use	■			None
(Patel et al., 2005)	Length of treatment	■			None
	Antipsychotic use		■		
	Dose		■		
(Chakos et al., 2006)	Antipsychotic use		■		None
(Dickey et al., 2006)	Dose		■		None
	High dose		■		
(Kelly et al., 2006)	Antipsychotic use	■			Clozapine use
	Dose			■	
(Mallinger et al., 2006)	Type (2nd generation)	■			Polypharmacy = FGA + SGAs
	Clozapine use	■			
	Polypharmacy	■			
(Valenstein et al., 2006)	Type (2nd generation)	■			Ziprasidone use
(Connolly et al., 2007)	Dose		■		None
	High dose		■		
	Polypharmacy		■		
	Type (2nd generation)		■		
	Cost			■	
(Gersing et al., 2007)	Type (2nd generation)		■		None

Reference	Outcome	Worse	No Difference	Better	Comments
(Kelly et al., 2007)	Clozapine cessation				None
(Kreyenbuhl et al., 2007b)	Polypharmacy				None
(Morrato et al., 2007)	Polypharmacy				None
(Connolly & Taylor, 2008)	Dose				None
	High dose				
	Type (1st generation)				
	Polypharmacy				
	Antipsychotic use				
	Type (2nd generation)				
	Polypharmacy - olanzapine depot plus oral				
(Busch et al., 2009b)	Medication quality (acute and maintenance)				Medication quality = dose, continuous supply
	Dose (acute and maintenance)				
	Antipsychotic use				
(Hanlon et al., 2009)	Antipsychotic use				None
	Type (2nd generation)				
	Polypharmacy				
(Pinto et al., 2010)	Depot use				None
	Type (2nd generation)				
	Antipsychotic use				
(Sleath et al., 2010)	Antipsychotic use				None

Reference	Outcome	Worse	No Difference	Better	Comments
(Connolly et al., 2011)	Dose		■		None
	High dose		■		
	Polypharmacy (2nd generation)		■		
	Type		■		
	Cost		■		
(Degenhardt et al., 2011)	Dose		■		None
(Rost et al., 2011)	Antipsychotic use			■	None
(Horvitz-Lennon et al., 2012)	Depot use		■		Risperidone long-acting injection
(Koranek et al., 2012)	Type (1st generation)	■			None
(Leslie & Rosenheck, 2012)	'Off label' use of SGAs			■	'Off label' = not for schizophrenia or bipolar
(Manuel et al., 2012)	Clozapine use	■			None
(Nejtek et al., 2012)	Dose		■		None
(Robst, 2012)	Antipsychotic use			■	None
	Dose	■			
	Polypharmacy		■		
	Cost	■			
(Dusetzina et al., 2013)	Type (2nd generation - olanzapine use)		■		None
(Horvitz-Lennon et al., 2013)	Clozapine use	■			Differences not tested statistically. *My analysis* (chi-squared) $p<0.01$ black vs. white.

Reference	Outcome	Worse	No Difference	Better	Comments
(Brown et al., 2014)	Depot use	■			None
(Stroup et al., 2014)	Clozapine use	■			None
(Kamble et al., 2015)	Stimulant and SGA use	■			None
(Lawson et al., 2015)	Antipsychotic use		■		None
	Oral SGA	■			
	Oral FGA	■			
	Depot SGA			■	
	Depot FGA	■			
(Cataife & Weinberg, 2015)	Antipsychotic use			■	None
(Burgio et al., 2016)	Antipsychotic prescribed		■		None
	Antipsychotic administration			■	None
(Herzig et al., 2016)	Antipsychotic use			■	None
(Cook et al., 2017)	Antipsychotic use (SGA)			■	None
(Das-Munshi et al., 2018)	Antipsychotic use		■		None
	Type of antipsychotic		■		
	Depot use	■			
	Clozapine use	■			
	High dose		■		
	Polypharmacy		■		
	Choice of antipsychotic		■		
	Written information		■		
	Benefits/side effects		■		

Black vs. non-black (reference category)

Reference	Outcome	Worse	No Difference	Better	Comments
(Tunnicliffe et al., 1992)	Dose of depot				Non-Caribbean assumed white
(Segal et al., 1996)	Antipsychotic use				Non-black = white, Asian, Hispanic, other ethnicities
	Dose				
	Depot use				
	Doses of antipsychotic				
	Antipsychotic injection number				
(Valenstein et al., 2001a)	Low dose (<300mg CPZe)				Non-black were other ethnicities (no other details)
(Mark et al., 2003)	Type (1st generation)				None
	Type (2nd generation)				
	Clozapine use				
	Depot use				
	Anticholinergic agent use				
(Woods et al., 2003)	Type (2nd generation)				Non-black = white, Hispanic, other
	Depot use				
	Polypharmacy				
(Van Dorn et al., 2005)	Type (2nd generation)				Non-black = white/other

Reference	Outcome	Worse	No Difference	Better	Comments
(Garver et al., 2006)	Type (2nd generation)			■	Polypharmacy classed as two 2nd generation antipsychotics
	Type (1st generation)		■		
	Polypharmacy (two 2nd generation antipsychotics)		■		
(Kilbourne & Pincus, 2006)	Type (1st generation)	■			None
	Type (2nd generation)		■		
	Antipsychotic use	■			
(Shi, 2007)	Depot use	■			Non-black = other (not white)
(Jin et al., 2010)	Dose		■		None
(Linares et al., 2013)	Type (2nd generation)	■			Non-black = mixed other (Asian, white)
(Puyat et al., 2013)	Antipsychotic use		■		None
	Type (2nd generation)	■			
(Brown et al., 2014)	Depot use	■			Non-black = other
(Kamble et al., 2015)	Stimulant and SGA use		■		Non-black = other
(McCutcheon et al., 2015)	Antipsychotic plasma levels	■			Non-black = white and other

White vs. non-white (reference category)

Reference	Outcome	Worse	No Difference	Better	Comments
(Lehman & Steinwachs, 1998)	Antipsychotic use				Non-white were black and other, analysed as white vs. Minority
	Dose				
	High dose				
	Length of treatment				
	Depot use				
	Anticholinergic agent use				
(Wang et al., 2000)	Type (2nd generation)				Non-white = other ethnicity
(Owen, 2001)	Type (2nd generation)				Non-white were black, Hispanic, Asian/Pacific Islanders
(Valenstein et al., 2001a)	High dose				Non-white =. other (no further details)
	Low dose (<300mg CPZe)				
(Covell et al., 2002)	Type (2nd generation)				Non-white = black and Hispanic
	Depot use				
(Luo et al., 2002)	Type (2nd generation)				Non-white = not stated
(Pinninti et al., 2003)	Type (2nd generation)				None
(Szarek & Goethe, 2003)	Antipsychotic use				Non-white = black and Hispanic
(Taylor et al., 2003)	Clozapine use				Non-white =black, Asian, mixed

Reference	Outcome	Worse	No Difference	Better	Comments
(Valenti et al., 2003)	Type (1st generation)				Non-white = black + other
(Mace & Taylor, 2005)	Dose				None
	High dose				
	Polypharmacy				
(Staller et al., 2005)	Antipsychotic use				None
(Olfson et al., 2006)	Antipsychotic use				Non-white = other
(Valenstein et al., 2006)	Type (2nd generation)				Ziprasidone use. Non-white = other (Asian, native American)
(Kreyenbuhl et al., 2007b)	Polypharmacy				Non-white = other ethnicity
(Shi, 2007)	Depot use				Non-white = other (not black)
(Jano et al., 2008)	Type (2nd generation)				None
(West et al., 2008)	Depot use				None
(Yang et al., 2008)	Type (2nd generation)				Non-white = other (American Indian, native Hawaiian, Asian, Pacific Islander)
(Constantine et al., 2010b)	Polypharmacy				Non-white = other
(Sleath et al., 2010)	Antipsychotic use				Non-white = Unknown race
(Wittkampf et al., 2010)	Antipsychotic use				Non-white = Moroccan or Turkish
(Findling et al., 2011)	Antipsychotic use				Non-white = other

Reference	Outcome	Worse	No Difference	Better	Comments
(Valenstein et al., 2006)	Type (2nd generation)				Ziprasidone use. Non-white = other (Asian, native American)
(Kreyenbuhl et al., 2007b)	Polypharmacy				Non-white = other ethnicity
(Shi, 2007)	Depot use				Non-white = other (not black)
(Jano et al., 2008)	Type (2nd generation)				None
(West et al., 2008)	Depot use				None
(Yang et al., 2008)	Type (2nd generation)				Non-white = other (American Indian, native Hawaiian, Asian, Pacific Islander)
(Constantine et al., 2010b)	Polypharmacy				Non-white = other
(Sleath et al., 2010)	Antipsychotic use				Non-white = Unknown race
(Wittkampf et al., 2010)	Antipsychotic use				Non-white = Moroccan or Turkish
(Findling et al., 2011)	Antipsychotic use				Non-white = other
(Puyat et al., 2011)	Antipsychotic use				Non-white = mixed
(Puyat et al., 2011)	Antipsychotic use				Non-white = non-white/non-Asian
(Rost et al., 2011)	Antipsychotic use				Non-white = other.
*(Aggarwal et al., 2012a)**	Depot use				None
	Type of depot (2nd generation)				

Reference	Outcome	Worse	No Difference	Better	Comments
(Coury et al., 2012)	Type (2nd generation)				Non-white = non-Caucasian
(Cruz et al., 2012)	Antipsychotic use				Non-white = immigrants (Eastern Europe, Mahgreb, Latin America, Africa)
	Type (not stated)				
(Fastenau et al., 2012)	Depot use				Non-white = other – no details
(Howes et al., 2012)	Delay in clozapine use				Non-white = black, Asian, mixed other
(Koranek et al., 2012)	Type (1st generation)				Non-white = other
(Robst, 2012)	Antipsychotic use				Non-white = other
	Dose				
	Polypharmacy				
	Cost				
(Hassan et al., 2013)	Dose				Non-white = non-white European
(Teo et al., 2013)	Polypharmacy				Non-white = non-white European
	Clozapine use				
	Clozapine polypharmacy				
(Rodday et al., 2014)	'Off label' 2nd generation antipsychotic use				Non-white = other
(Stroup et al., 2014)	Clozapine use				Non-white = other

Reference	Outcome	Worse	No Difference	Better	Comments
(Stevenson et al., 2010)	Antipsychotic use				None
	Antipsychotic indication (appropriate; potentially appropriate; not appropriate)				

Asian vs. white (reference category)

Reference	Outcome	Worse	No Difference	Better	Comments
(Binder & Levy, 1981)	Dose				None
(Lin & Finder, 1983)	Dose				None
(Jann et al., 1992)	Dose				Asian = Chinese
(Collazo et al., 1996)	Dose				Asians = Chinese subjects
	Anticholinergic agent use				
(Matsuda et al., 1996)	Dose (clozapine)				None
(Taylor, 2004)	Dose				None
	Polypharmacy (with clozapine)				
	Polypharmacy (with olanzapine)				
(Ng et al., 2005)	Dose clozapine				Clozapine use
(Morrato et al., 2007)	Polypharmacy				None
(Hashmi et al., 2009)	Switching from FGAs to SGAs				None
(Puyat et al., 2011)	Antipsychotic use				Asian = Chinese
(Puyat et al., 2011)	Antipsychotic use				Asian = other Asian

Reference	Outcome	Worse	No Difference	Better	Comments
(Cataife & Weinberg, 2015)	Antipsychotic use				None
(Das-Munshi et al., 2018)	Antipsychotic use				None
	Type of antipsychotic				
	Depot use				
	Clozapine use				
	High dose				
	Polypharmacy				
	Choice of antipsychotic				
	Written information				
	Benefits/side effects				

Asian vs. black (reference category)

Reference	Outcome	Worse	No Difference	Better	Comments
(Binder & Levy, 1981)	Dose				None
(Jann et al., 1992)	Dose				Asian = Chinese

Asian vs. Hispanic (reference category)

Reference	Outcome	Worse	No Difference	Better	Comments
(Jann et al., 1992)	Dose				Asian = Chinese
(Collazo et al., 1996)	Dose				Asians = Chinese subjects
	Anticholinergic agent use				
(Ruiz et al., 1996)	Dose				None

Asian vs. non-Asian (reference category)

Reference	Outcome	Worse	No Difference	Better	Comments
(Lin et al., 1996)	Dose				Non-Asian = white, black, Hispanic)
(Ruiz et al., 1996)	Dose				Non-Asian = general i.e. not Asian and not Hispanic
	Anticholinergic agent use				

Mixed vs. white (reference category)

Reference	Outcome	Worse	No Difference	Better	Comments
(Das-Munshi et al., 2018)	Antipsychotic use				None
	Type of antipsychotic				
	Depot use				
	Clozapine use				
	High dose				
	Polypharmacy				
	Choice of antipsychotic				
	Written information				
	Benefits/side effects				

Chinese/Other vs white (reference category)

Reference	Outcome	Worse	No Difference	Better	Comments
(Das-Munshi et al., 2018)	Antipsychotic use				None
	Type of antipsychotic				
	Depot use				
	Clozapine use				
	High dose				
	Polypharmacy				
	Choice of antipsychotic				
	Written information				
	Benefits/side effects				

Hispanic vs. white (reference category)

Reference	Outcome	Worse	No Difference	Better	Comments
(Adams et al., 1984)	Dose				None
	Polypharmacy				
(Jann et al., 1992)	Dose				None
(Collazo et al., 1996)	Dose				None
	Anticholinergic agent use				
(Ruiz et al., 1999)	Dose				None
(Baillargeon & Contreras, 2001)	Type of antipsychotic (2^{nd} generation)				None
(Leslie & Rosenheck, 2001)	Dose				None
	Polypharmacy				

Reference	Outcome	Worse	No Difference	Better	Comments
*(La*sser et al., 2002)					Visit rates for antipsychotic prescription
(Copeland et al., 2003)	Type (2nd generation)				None
	Clozapine use				
(Daumit et al., 2003)	Type (2nd generation)				None
(Bagchi et al., 2004)	Type (2nd generation)				None
	Antipsychotic use				
(Leslie & Rosenheck, 2004)	Dose				None
	High dose				
(Valenstein et al., 2006)	Type (2nd generation)				Ziprasidone use
(Kreyenbuhl et al., 2007b)	Polypharmacy				None
(Morrato et al., 2007)	Polypharmacy				None
(Tamayo et al., 2007)	Dose				None
(Depp et al., 2008)	Antipsychotic use				None
(Yang et al., 2008)	Type (2nd generation)				None
(Busch et al., 2009a)	Antipsychotic use				None
(Busch et al., 2009b)	Medication quality (acute and maintenance)				Medication quality = dose, continuous supply
	Dose (acute and maintenance)				
(Constantine et al., 2010b)	Polypharmacy				None

Reference	Outcome	Worse	No Difference	Better	Comments
(Rost et al., 2011)	Antipsychotic use				None
(Horvitz-Lennon et al., 2012)	Depot use				Risperidone long-acting injection
(Koranek et al., 2012)	Type (1st generation)				None
(Leslie & Rosenheck, 2012)	'Off label' use of SGAs				'Off label' = not for schizophrenia or bipolar
(Manuel et al., 2012)	Clozapine use				None
(Robst, 2012)	Antipsychotic use				None
	Dose				
	Polypharmacy				
	Cost				
(Dusetzina et al., 2013)	Type (2nd generation - olanzapine use)				None
(Horvitz-Lennon et al., 2013)	Clozapine use				Difference not tested statistically. *My analysis* (chi-squared) Latino vs. white $p<0.01$.
(Stroup et al., 2014)	Clozapine use				None
(Cataife & Weinberg, 2015)	Antipsychotic use				None
(Cook et al., 2017)	Antipsychotic use (SGA)				None

Hispanic vs. black (reference category)

Reference	Outcome	Worse	No Difference	Better	Comments
(Adams et al., 1984)	Dose		■		None
	Polypharmacy			■	
(Jann et al., 1992)	Dose	■			None
(Ruiz et al., 1999)	Dose			■	None
(Jaffe & Levine, 2003)	Polypharmacy			■	None
(Linares et al., 2013)	Type (2nd generation)			■	None

Hispanic vs. non-Hispanic (reference category)

Reference	Outcome	Worse	No Difference	Better	Comments
(Ruiz et al., 1996)	Dose			■	Non-Hispanic = general i.e. not Hispanic not Asian
(Covell et al., 2002)	Type (2nd generation)	■			None
	Polypharmacy			■	
				■	
(Aggarwal et al., 2012b)	Polypharmacy (depot plus oral)	■			Non-Hispanic not defined. Other groups black, white, other. Hispanic included mixed.
(Coury et al., 2012)	Type (2nd generation)	■			None
(Puyat et al., 2013)	Antipsychotic use		■		None
	Type (2nd generation)	■			

Mexican American vs. white (reference category)

Reference	Outcome	Worse	No Difference	Better	Comments
(Opolka et al., 2003)	Type (2nd generation) 1st 10 months				None
	Type (2nd generation) 2nd 10 months				
(Opolka et al., 2004)	Type (2nd generation)				None

American Indian vs. white (reference category)

Reference	Outcome	Worse	No Difference	Better	Comments
(Ferguson et al., 2006)	Antipsychotic use				None
(Cataife & Weinberg, 2015)	Antipsychotic use				Ethnic group American Indian /Alaska Native.

Maori vs. Non-Maori (reference category)

Reference	Outcome	Worse	No Difference	Better	Comments
(Metcalfe et al., 2013)	Type (2nd generation oral)				None
	Depot (1st generation)				
(Dey et al., 2016)	Antipsychotic dose (CPZe)				Non-Maori = New Zealand European, Asian, Pacific Islander and other.
	Type (not stated)				
	Route (not stated)				
	Clozapine use				

Asian, Maori and Pacific Islanders vs. Non-Ethnic Minority (reference category)

Reference	Outcome	Worse	No Difference	Better	Comments
(Puyat et al., 2013)	Antipsychotic use				None

Hawaiian or multiracial vs. white (reference category)

Reference	Outcome	Worse	No Difference	Better	Comments
(Cataife & Weinberg, 2015)	Antipsychotic use				None

Unclassifiable Papers

Authors	Number	Ethnicity	Type of study	Location	Medication Outcomes	Results	Comments
(Varner et al., 2001)	153	African American, Euro-American, Hispanic, Asian American	Retrospective cohort	USA	Dose	No difference by ethnicity in oral dose or depot use ($p>0.05$). No further details.	None
(Lelliott, 2002)	3576	Black, white, Asian, other	Survey	UK	Antipsychotic polypharmacy and high dose	No effect of ethnicity on either outcome. No further details.	None
(Moore et al., 2002)	132	East Indian, African, mixed	Survey	Trinidad	Psychotropic drug use	No differences in prescribing of antipsychotic medication by ethnicity. No further details.	African and East Asian patients were prescribed SSRI-type antidepressants less often than mixed patients ($p=0.005$).

Authors	Number	Ethnicity	Type of study	Location	Medication outcomes	Results	Comments
(Ciliberto et al., 2005)	439	Black, white. Other	RCT	USA	Efficacy (change in PANSS score), adverse effects (Extrapyramidal Symptom Rating Scale) and discontinuation rates of risperidone long-acting injection vs. placebo	No difference by race in dose, efficacy, tolerability and discontinuation. No further details.	None
(Pogge et al., 2007)	309	White, black, Hispanic, other	Case control study	USA	Receipt of SGA vs. no antipsychotic	No difference by ethnicity in use of SGA vs. no antipsychotic (p=0.08).	Adolescents.
(Domino & Swartz, 2008)	Not stated specifically (database of 23 000 - 35 000 subjects)	Black, white, Hispanic	Survey comparing data from 1996-7 to 2004-5.	USA	Prevalence of antipsychotic prescribing; characteristics of antipsychotic users	No difference between ethnicities in probability of antipsychotic medication use (no values quoted).	None

Authors	Number	Ethnicity	Type of study	Location	Medication outcomes	Results	Comments
(Grossman et al., 2008)	750	African American, white, other	Randomised Controlled Trial	USA	Functional genetic variation in drug metabolising enzymes (DME) and effect on dose, efficacy and safety of antipsychotics.	No effect of genetic variation in DME and dosing, efficacy and safety (including tardive dyskinesia) for olanzapine, perphenazine, quetiapine, risperidone, ziprasidone.	Analysis of CATIE study group.
(Thorens et al., 2008)	92	Swiss, EU, non-EU	Questionnaire	Switzerland	Receipt of an antipsychotic	No difference by ethnicity in receipt of an antipsychotic p=0.26, no further details.	Patients defined by country of origin, Poland and Romania included in non-EU countries.

Authors	Number	Ethnicity	Type of study	Location	Medication outcomes	Results	Comments
(Wheeler et al., 2008)	4821	European, New Zealand Maori, Pacific Islander, Asian	Survey	New Zealand	Antipsychotic polypharmacy, type, route, dose, clozapine use at 2 time points (baseline time (T1) in 2001 and time (T2) in 2004)	Antipsychotic monotherapy= numerical differences at T1 between ethnic groups but not at T2; type = SGA use increased, FGA use decreased, no differences between ethnicities at T2; route = depot use decreased - no differences between ethnicities at T2; clozapine = Asian patients less likely to receive than other ethnicities; dose = significant difference between ethnicities at both T1 and T2 (lowest mean dose Asian, highest Maori).	Statistical differences between T1 and T2 measured, not between ethnic groups.
(Wheeler, 2008)	2796	European, New Zealand Maori, Pacific Nations, Asian, other	Survey	New Zealand	Clozapine use	Clozapine use differed by ethnicity (p=0.002).	None
(Barnes et al., 2009)	1715	White, black, Asian, Chinese, mixed, other	Re-analysis of data from 3 audits	UK	Use of long-acting antipsychotic injections	No association between use of antipsychotic long-acting injections and ethnicity. No further information.	

Authors	Number	Ethnicity	Type of study	Location	Medication outcomes	Results	Comments
(Ponto et al., 2010)	371	Malay, Chinese, Indian	Cross-sectional survey	Malaysia	Dose (CPZe)	No differences in dose by ethnicity (actual values not stated).	
(Douzenis et al., 2011)	153	Greek, non-Greek	Observational study	Greece	Treatment outcome (GAF, BPRS), polypharmacy, type of antipsychotic	No significant differences for treatment outcome, polypharmacy and type of antipsychotic (chi-squared and Mann Whitney analysis).	Most of immigrant group were Albanian (32 of 63).
(el-Badri & Mellsop, 2011)	201	Maori, European, other	Database study	New Zealand	Dose, length of treatment, number of hospitalisations of clozapine	No differences in these outcomes by ethnicity. No further information.	None
(Arnold et al., 2013)	722	Non-Hispanic whites, African-Americans, Hispanics	Randomised trial	USA	Dose of antipsychotic	Prescribed daily dose differed by ethnicity (which one not stated) for risperidone only (not other antipsychotics) (p=0.04). Non-Hispanic whites had the highest average dose (4.4mg) followed by African Americans (4mg) then Hispanics (3.9mg).	None

Authors	Number	Ethnicity	Type of study	Location	Medication outcomes	Results	Comments
(Velligan et al., 2015)	2919	White, black, other	Survey	USA	Outcomes of clozapine use vs. antipsychotic polypharmacy	Fewer white vs. non-white patients in clozapine monotherapy group vs. polypharmacy group (52% vs. 61%, no p value). Polypharmacy group differs by race/ethnicity (not specified which) from clozapine group ($p<0.001$).	None
(Moore & Mattison, 2017)	40.4 million	White/other, black, Asian, Hispanic	Survey	USA	Psychotropic use (including antipsychotics)	Antipsychotics used for white 1.7%, black 1.9%, Asian 0.7% and Hispanic 1.3%. White patients used psychotropics more frequently than Hispanic (OR 3.1, 95% CI 2.7, 3.5) but not Asian (vs. Hispanic) or black (vs. Hispanic).	Sample size for all psychotropics. Numerical analysis only for antipsychotics.

Authors	Number	Ethnicity	Type of study	Location	Medication outcomes	Results	Comments
(Tang et al., 2017)	650	Hispanic, non-Hispanic black	Cohort study	USA	Clozapine use, antipsychotic polypharmacy (≥90 days, non-clozapine combinations)	Prescribers with higher percentages of ethnic minority patients were less likely to prescribe clozapine and polypharmacy than those with lower percentages. Hispanic patients clozapine use (OR 0.97, 95% CI 0.96, 0.98, p=0.001), polypharmacy use (OR 0.99, 95% CI 0.98, 0.99, p<0.001). Non-Hispanic black clozapine (OR 0.99, 95% CI 0.99. 0.99,p<0.001) polypharmacy (OR 1.00, 95% CI 0.99,1.00, p<0.05).	Compared prescribing for prescribers with high and low proportions of ethnic minorities not vs. another ethnic group.

* same dataset; B= black; BPAD = bipolar affective disorder; BPRS = Brief Psychiatric Rating Scale; CATIE = Clinical Antipsychotic Trials for Intervention Effectiveness; CGI-S = Clinical Global Impression – Severity; CI = confidence interval; CPZe = chlorpromazine equivalents; EPSE = extrapyramidal side effects; GAF = Global Assessment of Functioning; IM = intramuscular ; PANSS = Positive and Negative Syndrome Scale; PORT = Patient Outcomes Research Team; RCT = randomised controlled trial; RR = risk ratio; RLAI = risperidone long-acting injection; SUD = substance misuse disorder; UK = United Kingdom; United States of America = USA.

APPENDIX 5 DATA COLLECTION FORM, ETHNICITY STUDY 1

Patient Details

Hospital No., patient initials and unit	**Age**	**Gender (M or F)**	**Smoking status (S or NS)**	**Socio-economic status**		**Ethnic Origin** *(self ascribed)* **Parental origin**	**First language**	**Height (metres) and weight (Kg)**	**Significant physical illness**	**Forensic history Y/N**
				Employment (E or UE)	***Education (GCSE, A, Degree)***					

Abbreviations: M = male, F= female ; S = smoker NS = non-smoker ; E = employed, UE = unemployed ; A = Advanced level

Mental State

Current diagnosis (ICD 10 coding)	**Current Mental Health Act section**	**Duration of illness** (in years, to 1 decimal place)	**Number of previous Admissions (1, 2-5, >5)**	**Length of current admission (days)**	**History/ actual substance abuse Y/N**	**History of non-compliance Y/N**

Drug Therapy – Current antipsychotic therapy**

Antipsychotic 1		**Antipsychotic 2**		**Antipsychotic 3**		**Total dose (% max)** (add 1+2+3)	**On regular anticholinergic? (Y/N)**
Drug dose (mg/day)	**Drug dose (% max)**	**Drug dose (mg/day)**	**Drug dose (% max)**	**Drug dose (mg/day)**	**Drug dose (% max)**		

** Count regular and prn. For prn record amount given in last full day. If more than 3 antipsychotics, add together all maxima and put in brackets the number of antipsychotics prescribed.

Drug Therapy – other factors

Had this treatment before Y/N	Other drug therapy (including alternative therapies)	Length of current antipsychotic treatment (days)

Drug Therapy – other factors continued

Previous antipsychotic treatment (names of drugs)	Cost of current treatment (as per BNF)	Patient influence on drug choice (Y/N)	Pros/cons discussed (Y/N)

Original Papers

Psychopharm

Journal of Psychopharmacology
21(2) (2007) 191–197

ISSN 0269-8811
SAGE Publications Ltd,
Los Angeles, London,
New Delhi and Singapore
10.1177/0269881107065899

Antipsychotic prescribing quality and ethnicity – a study of hospitalized patients in south east London

Anne Connolly *Pharmacy Department, Maudsley Hospital, London, UK.*
Paul Rogers *School of Care Sciences, University of Glamorgan, Pontypridd, UK.*
David Taylor *Pharmacy Department, Maudsley Hospital, London, UK.*

Abstract

A number of studies have shown qualitative and quantitative differences in prescribing of antipsychotics according to patient ethnicity. Black patients tend, for example, to be prescribed higher doses of antipsychotics than whites. Few studies have controlled for other factors which may influence prescribing practice and confound results. This study sought to determine whether or not ethnicity was associated with antipsychotic polypharmacy, high dosage and antipsychotic costs before and after adjustment for potential confounding.

We approached inpatients on acute general psychiatry wards at the Maudsley, Bethlem and Lambeth hospitals in south east London. Prescription details were noted. Subjects were interviewed and social and clinical details were recorded. In all, data on 23 potential confounders were collected.

A total of 210 patients were approached of whom 153 agreed to take part. Of the 23 potential confounders, only use of English as a first language and duration of illness differed significantly between blacks and whites. Categorical findings were adjusted for these factors and other potential confounders such as age and gender. Total antipsychotic daily dose was 82.2% of licensed maximum in blacks, and 77.2% in whites ($p = 0.48$). Antipsychotic polypharmacy was seen in 23.2% of blacks and 16.9% of whites (adjusted odds ratio (OR) 1.11; 95% CI, 0.45–2.75). High dose (> 100% of maximum dose) antipsychotic regimens were prescribed to 15.9% of blacks and 16.9% of whites (adjusted OR, 0.71: 95% CI, 0.27–1.90). Mean monthly cost of treatment was significantly higher in blacks than whites (£182.79 vs £143.08; $p = 0.02$; adjusted OR (> £150/month), 2.45: 95% CI, 1.19–5.08).

Prescribing quality was similar for blacks and whites. Black ethnicity was associated with significantly higher mean monthly medication costs.

Keywords

antipsychotics, prescribing, race, polypharmacy

Introduction

Over many years it has frequently been suggested that the drug treatment of illness in black people (African-Americans, Africans, Afro-Carribeans) in Western societies differs importantly from that of white people (Ball and Elixhauser, 1996; Claiborne-Johnson *et al*., 2001; Kressin and Petersen, 2001). In psychiatry, several studies have shown that black people with schizophrenia or bipolar illness are prescribed different doses and types of antipsychotics compared with white patients (Flaskerud and Hu, 1992; Segal *et al*., 1996; Fleck *et al*., 2002; Kuno and Rothbard, 2002). Most of these studies have investigated African-American patients and concluded that black Americans receive larger doses of both antipsychotics in general (Segal *et al*., 1996; Walkup *et al*., 2000; Diaz and de Leon, 2002) and depot antipsychotic medications in particular (Kuno and Rothbard, 2002; Kreyenbuhl *et al*., 2003) and are less likely to be treated with some atypical antipsychotics (Kuno and Rothbard, 2002; Copeland *et al*., 2003; Daumit *et al*., 2003; Kreyenbuhl *et al*., 2003; Opolka *et al*., 2003).

The majority of these studies were conducted in the United States. The largest studies (some including tens of thousands of patients) used information from databases such as Medicaid and the Automated Information System. Smaller studies (prospective or retrospective prescribing surveys) generally collected more demographic and patient details. These demographic and patient data are important because there are a great many potential influences on prescribing practice. Examples include diagnosis, body weight and duration of illness. Without comparing other possible

Corresponding author: David Taylor, Pharmacy Department, Maudsley Hospital, London, UK. *Email*: david.taylor@slam.nhs.uk

influences on prescribing it is inappropriate to draw conclusions about the precise influence of race: there may be confounding factors which explain observed differences in practice.

In this study, we sought to address some of the shortfalls of previous studies by comparing prescribing practices in black and white patients, while collecting comprehensive details of patient and clinical factors felt likely to influence prescribing practice. Our aim was to compare prescribing by ethnicity alone by exclusion of other potential confounding influences.

Method

This study was conducted at the South London and Maudsley NHS Trust during 2003 and 2004. The Trust's ethics committee approved the study. Patients included were black or white and had been taking the same antipsychotic for 3 weeks or longer at the time of recruitment. Patients were classed as black if both parents were also black (including Africans, African-Americans and Afro-Caribbeans). Mixed race patients were excluded. Each patient was provided with an information sheet about the study and asked to give written consent. Data on gender, age and race were recorded for patients who did not wish to participate in the study. All suitable patients in three acute hospitals were approached over a 3 month period: none was excluded except for reasons above.

Data collection

One of us (Anne Connolly) approached patients and interviewed them. Patients self-reported their and their parents' ethnic origins. The outcomes of dose, being prescribed antipsychotic medication above maximum dose, polypharmacy (the concurrent prescription of two antipsychotics) and costs were determined by reference to each patient's medication chart and to standard reference texts for dose and cost (British National Formulary and Monthly Index of Medical Specialities respectively).

Potential confounders were predetermined. We searched all retrieved published papers on the subject and noted all potential confounders previously examined and included these. In addition we considered other patient details which were available to us and might conceivably influence prescribing practice and included these, too. They were: age (determined by reference to case notes), gender (self-report), smoking status (self-report with confirmation from nursing staff), diagnosis (case notes), employment status (self-report), education (self-report with confirmation from case notes), first language (self-report), height (measured), weight (measured), body mass index (calculated), forensic history (case notes), current legal status (case notes), duration of illness (case notes), number of previous admissions (case notes), length of current admission (case notes), history of or current substance misuse (case notes with confirmation from nursing staff), history of non-compliance (case notes), previous treatment with current antipsychotic medication (case notes), anticholinergic prescribed regularly (prescription chart), length of current antipsychotic treatment (prescription chart), previous antipsychotic treatment (case notes), patients recalling choice of drug (self-report), patients recalling receiving drug information (self-report).

Statistical analysis

Justification for sample size We performed a 'power' calculation before starting the study. A sample size of 142 was calculated to be required to give an 80% chance of detecting a 10% absolute difference for our outcome of interest (mean maximum dose) between white and black patients ($\alpha = 0.05$, $\sigma = 30$).

Data analysis Data collected were analysed as follows: interval and ratio data were compared using a two-tailed, unpaired Student's t-test (assuming normal distribution); categorical data were compared using chi-square tests. This allowed us to determine which variables were potentially confounding any observed association between ethnicity and the three outcomes of interest. As is conventional, all associations were adjusted for age and gender. Where an association was observed between ethnicity and a potential confounder then unadjusted and adjusted odds ratios (with 95% confidence intervals) were calculated through logistic regression using Stata 7. The basis of our method for adjusting for the influence of confounders was that true confounders were required to show an association both between outcome (dose of antipsychotic) and exposure (ethnicity). Potential confounders not significantly associated with ethnicity were assumed to influence (or not to influence) outcome to the same degree in both groups and so no adjustment was made.

Results

We approached 210 patients (all patients present on study wards) and 153 gave written informed consent. Of those 57 patients who declined to take part, 41 (71.9%) were black, 32 (56.1%) were male and the mean age was 40.9 years. Of those 153 who took part, 82 (53.6%) were black and 71(46.4%) were white. Black patients were significantly over-represented in those declining to take part ($\chi^2 = 6.93$, df = 1, $p = 0.01$).

There were no differences between blacks and whites in respect to: polypharmacy (Table 1) or being prescribed antipsychotic medication above maximum dose (Table 1), or mean maximum dose (Table 2). There was no difference in type of antipsychotic prescribed (Table 4). A positive association was observed between black ethnicity and greater mean monthly antipsychotic medication costs ($p = 0.02$) (Table 1). Of the 24 potential confounders (including co-morbid diagnosis – Table 3), only two were associated with ethnicity: English as a first language ($p = 0.03$) and duration of illness ($p = 0.01$) (Table 1). They were considered potential confounders and unadjusted and adjusted odds ratios (with 95% confidence intervals) were calculated. In addition, we considered age and ethnicity as potential confounders so adjusted for any effects these may be causing. Finally, when examining the odds ratios for each of the three outcomes we adjusted for any potential effect that the other two outcomes may be contributing.

Table 1 Associations between ethnicity, outcomes and potential confounders

	Black ($n=82$)	White ($n=71$)	p
OUTCOMES			
Polypharmacy	19 (23.2%)	12 (16.9%)	0.23
Mean monthly cost of current antipsychotic treatment *(MIMs January 2004)*	£182.79	£143.08	0.02*
Above maximum dosage	13 (15.9%)	12 (16.9%)	0.52
POTENTIAL CONFOUNDERS			
Mean age	37.8	40.3	0.21
Gender			
Male	56 (68.3%)	47 (66.2%)	0.55
Smoking status			
Smoker	64 (78%)	58 (81.7%)	0.5
Primary Diagnosis			
Schizophrenia/psychosis	58 (70.7%)	46 (64.7%)	0.46
Schizoaffective disorder	13 (15.8%)	10 (14.1%)	(psychosis vs. no
Bipolar affective disorder	8 (9.8%)	6 (8.5%)	psychosis)
Other	3 (3.7%)	9 (12.7%)	
Employment			0.5
Employed	4 (4.9%)	4 (5.6%)	(working vs. not working)
Unemployed	74 (90.2%)	66 (93%)	
Retired	3 (3.7%)	1(1.4%)	
Prison sentence	1(1.2%)	0	
Education			0.5
Primary school	2 (2.4%)	3 (4.2%)	(up to secondary school vs
Secondary school	54 (65.9%)	49 (69%)	post secondary school
A-level	16 (19.5%)	12 (16.9%)	education)
Degree level	5 (6.1%)	6 (8.5%)	
Don't know	5 (6.1%)	1 (1.4%)	
First language			
English	74 (90.2%)	70 (98.6%)	0.03*
Mean height (cm)	171.7	172.2	0.76
Mean weight (kg)	81.3	81.2	0.99
Mean Body Mass Index (BMI)	27.4	27.3	0.94
Forensic history	46 (56.1%)	40 (56.3%)	0.6
Current MHA section			
Informal	28 (34.2%)	34 (47.9%)	0.0825
Section 3	47 (57.3%)	31 (43.7%)	(informal vs. section)
Section 2	4 (4.9%)	2 (2.8%)	
Other e.g. 47/49, 35	3 (3.7%)	4(5.6%)	
Duration of illness (years)	12.6	15.7	0.01*
Number of previous admissions			
None	10 (12.2%)	5(7%)	0.55
1	9 (11%)	10 (14.1%)	(0–1 vs 2 or more)
2 to 5	21(25.6%)	19 (26.8%)	
>5	42(51.2%)	37 (52.1%)	
Length of current admission (days)	191.3	171.7	0.64
History of or current substance abuse	45 (54.9%)	43 (60.6%)	0.575
History of non-compliance	65 (79.3%)	59 (83%)	0.51
Previous treatment with current antipsychotic therapy	47 (57.3%)	49 (69%)	0.2
Patient prescribed an anticholinergic regularly	8 (9.8%)	11(15.5%)	0.36
Length of current antipsychotic treatment (days)	299	378	0.6
Previous antipsychotic treatment (n mean)	3.1	3.1	0.92
Patients recalling a drug choice	10 (12.1%)	11 (15.5%)	0.50
Patients recalling drug information	40 (48.8%)	25 (35.2%)	0.09

Table 2 Associations between ethnicity and drug dose

Drug type	Black ($n=82$)	White ($n=71$)	p
First antipsychotic drug dose (% maximum)	69.5	68.5	0.87
Second antipsychotic drug dose (% maximum)	12.7	8.7	0.18
Third antipsychotic drug dose (% maximum)	0	0	N/A
Total dose (% maximum)	82.2	77.2	0.48

Table 3 Co-morbid diagnosis

Ethnicity	Black ($n=82$)	White ($n=71$)
Number of subjects with co-morbid psychiatric diagnosis $\chi^2=1.5888$; df=1 ; $p=0.2075$	12*	16*
Co-morbid diagnoses:		
Anxiety disorder	1	1
Autism	1	2
Bipolar affective disorder	1	1
Delusional disorder	2	0
Dementia	0	1
Depression	1	4
Learning disability	5	1
Personality disorders	0	3
Psychosis	1	1
Substance misuse	1	4

*Patients may have more than one other co-morbid condition

Table 4 Drug type

Drug type	Black ($n=82$)	White ($n=71$)	p
First antipsychotic			
Atypical po (not clozapine)	45 (54.9%)	36 (50.7%)	0.55 (typicals vs atypicals)
Atypical im (depot)	9 (11%)	5 (7%)	0.525 (clozapine)
Typical po	2 (2.4%)	6 (8.5%)	
Typical im (depot)	11 (13.4%)	9 (12.7%)	
Clozapine	15 (18.3%)	15 (21.1%)	
Totals			
Atypical (including clozapine) po & im	69 (84.1%)	56 (78.9%)	
Typical po & im	13 (15.9%)	15 (21.1%)	
Second antipsychotic			
Atypical po (not clozapine)	8 (9.8%)	7 (9.9%)	0.5 (typicals vs atypicals)
Atypical im (olanzapine)	8 (9.8%)	2 (2.8%)	
Typical po	2 (2.4%)	2 (2.8%)	
Typical im (haloperidol)	1 (1.2%)	1 (1.4%)	
Clozapine	0	0	
Totals			
Atypical (including clozapine) po & im	16 (19.5%)	9 (12.7%)	
Typical po & im	3 (3.7%)	3 (4.2%)	
Third antipsychotic			
Drug type	0	0	N/A

For black ethnicity and polypharmacy there was no evidence of an association before (OR, 1.48; 95% CI, 0.66–3.22) or after adjustment for age, gender, duration of illness, English as a first language, diagnosis, being prescribed antipsychotic medication above maximum dose and medication costs (OR, 1.11; 95% CI, 0.45–2.75).

For black ethnicity and being prescribed antipsychotic medication above maximum there was no evidence of an association before (OR, 0.93; 95% CI, 0.39–2.18) or after adjustment for: age, gender, duration of illness, English as a first language, diagnosis, polypharmacy and medication costs (OR, 0.71: 95% CI, 0.27–1.90).

For black ethnicity and medication costs of above £150 per month there was a positive association before (OR, 2.39; 95% CI, 1.26–4.60) or after adjustment for: age, gender, duration of illness, English as a first language, diagnosis, polypharmacy and being prescribed antipsychotic medication above maximum dose (OR, 2.45: 95% CI, 1.19–5.08).

Blacks and whites did not differ significantly in type of antipsychotic prescribed (Table 4).

We also examined dose prescribed by calculating chlorpromazine equivalent dose (Table 5). There was no significant difference in dose prescribed by ethnicity.

Approximate mean monthly costs of the antipsychotics prescribed in this study are given in Table 6.

Discussion

Main findings

In this study overall prescribing quality did not differ between blacks and whites. Dose, type and number of antipsychotics prescribed for black and white patients were not statistically different. Numerical differences were small and there was no suggestion of clinically important differences in prescribing quality. Adjustment for the influence of confounders did not alter overall findings. The two groups had broadly similar clinical and patient characteristics. Only cost of antipsychotic drugs differed between groups.

Limitations

Before the study we calculated that a sample size of 142 would be required to give an 80% chance of detecting a 10% absolute difference in our outcomes of interest assuming a standard deviation of 30. The number of patients recruited exceeded our original target but standard deviation of percentage maximum dosage was greater than initially predicted. This decreased the power of our study to a small extent. In addition, our study did not have the power to detect smaller differences in mean dose, although the importance of absolute differences of less than 10% is debatable.

Of those who declined to take part in the study, black patients

Table 5 Associations between ethnicity and drug dose (as chlorpromazine equivalents)

Drug dose (chlorpromazine equivalents in mg/day)	Black ($n=82$)	White ($n=71$)	p
First antipsychotic drug dose	493.9	526.9	0.69
Second antipsychotic drug dose	69.5	50.5	0.47
Third antipsychotic drug dose	0	0	N/A
Total dose	563.4	577.4	0.90

(Woods 2003; American Psychiatric Association, 2004; Bazire S, 2005)

Table 6 Relative costs of antipsychotics

Antipsychotic drug	Cost of treatment (Jan 2004 28 days in £)	Approximate average clinical dose (mg/day)
Amisulpride tablets	123.20	800 mg/day
Clozapine tablets	197.12	400 mg/day
Flupentixol depot	13.44	80 mg/2 weekly
Haloperidol tablets	4.50	10 mg/day
Olanzapine tablets	146.34	15 mg/day
Pipothiazine depot	18.51	100 mg/month
Quetiapine tablets	132.11	400 mg/day
Risperidone tablets	109.20	6 mg/day
Risperidone long-acting injection	231.68	37.5 mg/2 weekly
Sulpiride tablets	20.32	800 mg/day
Trifluoperazine tablets	1.32	15 mg/day
Zuclopentixol depot	6.78	200 mg/2 weekly

were over-represented. This is not entirely unexpected given that black patients are less likely than white patients to participate in research (Shavers-Hornaday *et al*., 1997; Corbie-Smith *et al*., 1999). Nonetheless it is possible that prescribing quality differed in those declining to take part from those who did take part. If prescribing quality was worse in these patients, then over-representation of blacks amongst those refusing would inevitably conceal overall poorer prescribing in the total population. Finally, we did not assess each patient's mental state at the time of data collection. Illness severity at the time of prescribing is clearly a factor that could have affected prescribed dose and apparent prescribing quality.

We measured 23 potential confounders. Only two were associated with the exposure of ethnicity: English as a first language and duration of illness. We found no association between ethnicity and polypharmacy or prescription of above higher than 100% maximum doses after correcting for confounders. We did find an association between antipsychotic medication costs and ethnicity. Specifically that black ethnicity is associated with higher mean monthly costs, with black patients being approximately two and half times more likely to have medication costs over £150 compared with white patients. It is difficult to determine why black ethnicity was associated with greater mean monthly antipsychotic medication costs than white patients but more frequent prescription of IM atypicals specifically and atypicals in general to black patients may provide a partial explanation. Numerical difference in dose will also have affected the dose.

A further consideration is the type of patient included in the study. On average, subjects in this study might be described as sub-chronic, having been in hospital and prescribed antipsychotics for some time. Extrapolations cannot be made to other patient types or clinical environments.

Previous studies

Our study results differ from most others examining prescribing quality and race. There are occasional studies that have found no differences in doses (Kreyenbuhl *et al*., 2003) and types of antipsychotic prescribed (Pinninti *et al*., 2003; Woods *et al*., 2003), but most other studies have found differences in doses (Segal *et al*., 1996; Walkup *et al*., 2000; Diaz and de Leon, 2002), types of antipsychotics prescribed (Baillargeon and Contreras, 2001; Owen *et al*., 2001; Covell *et al*., 2002; Copeland *et al*., 2003; Daumit *et al*., 2003; Kreyenbuhl *et al*., 2003; Opolka *et al*., 2003) and rates of polypharmacy (Taylor, 2004). All of these studies indicated poorer prescribing quality in black patients. In addition some studies have found depots are more likely to be prescribed for black patents than whites (Covell *et al*., 2002; Kuno and Rothbard, 2002; Kreyenbuhl *et al*., 2003; Woods *et al*., 2003) although this was not seen in the present study. Because doses of depot antipsychotics are often higher than equivalent oral antipsychotic doses this may account for the high doses observed in black patients. This is particularly likely when depot doses are converted into chlorpromazine equivalents (Segal *et al*., 1996; Walkup *et al*., 2000). We found no differences in doses prescribed as assessed by percentage maximum dose and chlorpromazine equivalents.

Other studies examining antipsychotic dose and ethnicity used chlorpromazine equivalents as the main measure of dose magnitude. The derivation of values for chlorpromazine equivalents is less than clear and largely relies for its legitimacy on repetition. We preferred the mean maximum dose method because of its clearer derivation and its close link to the legalities of prescribing (Yorston and Pinney, 2000). It is possible that the two methods generate different results on comparison, but our calculations by these methods gave broadly similar results.

As we found no major differences in prescribing practice it is possible that prescribing quality differences may be less common in the UK or in more recent times. Most previous studies were conducted in the US where lack of health-care insurance for black patients may be a significant factor affecting the type and form of antipsychotic prescribed (Daumit *et al*., 2003). In the UK, very few of those with a severe mental illness pay prescription charges and no one pays for hospital treatment or drugs prescribed in hospital. Shorter engagement time during consultations (Segal et al., 1996), fewer contacts with mental health services and shorter lengths of follow-up after admission (Kuno and Rothbard, 2002) for black patients compared with whites are also important factors affecting prescribing quality which may not be relevant in the UK. In addition it is likely that the prevalence and strength of racist attitudes have declined in Western societies in recent times. The results of our study may thus be explained by the UK's apparent equality in health-care provision and temporal changes in attitude.

Despite the impressive sample sizes of some studies, researchers have examined few factors that might have affected apparent prescribing quality. All studies examined collected information on age, sex and race but the numbers of other factors studied ranged from only one (Baillargeon and Contreras, 2001; Owen *et al*., 2001) to up to ten (Kreyenbuhl *et al*., 2003). Most studies made no attempt to account for even these few confounders. Excluding age, sex and race we included over 20 other potentially confounding factors so rendering more robust our findings.

Implications of our findings

Our findings indicate that ethnicity does not affect antipsychotic prescribing quality for a cohort of patients in the South London and Maudsley NHS Trust. The robust research method allows us to be relatively confident that confounding factors have not affected our results.

Acknowledgements

We wish to thank Professor Dinesh Bhugra for his advice on the design and reporting of this study.

This study was funded by a grant awarded by the health service research committee of the South London and Maudsley NHS trust.

References

American Psychiatric Association (2004) Practice Guideline for the Treatment of Patients With Schizophrenia, second edition. American Journal of Psychiatry *161* (suppl. 2): 1–56

Baillargeon J, Contreras S A (2001) Antipsychotic prescribing patterns in the Texas prison system. Journal of the American Academy of Psychiatry and the Law *29*: 48–53

Ball J K, Elixhauser A (1996) Treatment differences between blacks and whites with colorectal cancer. Medical Care *34*, 970–984

Bazire S (2005) Psychotropic Drug Directory: The Professionals' Pocket Handbook and Aide Memoire. Fivepin Limited, Salisbury, UK

Claiborne-Johnson S, Fung L H, Gillum L A, Smith W S, Brass L M, Lichtman J H, Brown A N (2001) Utilization of intravenous tissue-type plasminogen activator for ischemic stroke at academic medical centres. The influence of ethnicity. Stroke *32*: 1061–1068

Copeland L A, Zeber J E, Valenstein M, Blow F C (2003) Racial disparity in the use of atypical antipsychotic medications among veterans. American Journal of Psychiatry *160*: 1817–1822

Corbie-Smith G, Thomas S B, Williams M V, Moody-Ayers S (1999) Attitudes and beliefs of African-Americans toward participation in medical research. Journal of General Internal Medicine *14*: 537–46

Covell N H, Jackson C T, Evans A C, Essock S M (2002) Antipsychotic prescribing practices in Connecticut's public mental health system: rates of changing medications and prescribing styles. Schizophrenia Bulletin *28*: 17–29

Daumit G L, Crum R M, Guallar E, Powe N R, Primm A B, Steinwachs D M, Ford D E (2003) Outpatient prescriptions for atypical antipsychotics for African Americans, Hispanics and Whites in the United States. Archives of General Psychiatry *60*: 121–128

Diaz F J, de Leon J (2002) Excessive antipsychotic dosing in two US state hospitals. Journal of Clinical Psychiatry *63*: 998–1003

Flaskerud J H, Hu L (1992) Race/ethnic identity and amount and type of psychiatric treatment. American Journal of Psychiatry *149*: 379–384

Fleck D E, Hendricks W L, Del Bello M P, Strakowski S M (2002) Differential prescription of maintenance antipsychotics to African American and white patients with new-onset bipolar disorder. Journal of Clinical Psychiatry *63*: 658–664

Kressin N R, Petersen L A (2001) Racial differences in the use of invasive cardiovascular procedures: review of the literature and prescription for future research. Annals of Internal Medicine *135*: 352–366

Kreyenbuhl J, Zito J M, Buchanan R W, Soeken K L, Lehman A F (2003) Racial disparity in the pharmacological management of schizophrenia. Schizophrenia Bulletin *29*, 183–193

Kuno E., Rothbard A B (2002) Racial disparities in antipsychotic prescription patterns for patients with schizophrenia. American Journal of Psychiatry *159*: 567–572

Opolka J L, Rascati K L, Brown C M, Barner J C, Johnsrud M T, Gibson P J (2003) Ethnic differences in use of antipsychotic medication among Texas Medicaid clients with schizophrenia. Journal of Clinical Psychiatry *64*: 635–639

Owen R R, Feng W, Thrush C R, Hudson T J, Austen M A (2001) Variations in prescribing practices for novel antipsychotic medications among veterans affairs hospitals. Psychiatric Services *52*: 1523–1525

Pinninti N R, Shaila B, Kumar G (2003) Racial bias in the prescription of atypical antipsychotics. Psychiatric Services *54*: 110

Segal S P, Bola J R, Watson M A (1996) Race, quality of care and antipsychotic prescribing practices in psychiatric emergency services. Psychiatric Services *47*: 282–286

Shavers-Hornaday V L, Lynch C F, Burmeister L F, Torner J C (1997) Why are African-Americans under-represented in medical research studies? Impediments to participation. Ethnicity and Health *2*: 31–45

Taylor D M (2004) Prescribing of clozapine and olanzapine: dosage, polypharmacy and patient ethnicity. Psychiatric Bulletin *28*: 241–243

Walkup J T, McAlpine D D, Olfson M, Labay L E, Boyer C, Hansell S (2000) Patients with schizophrenia at risk of excessive antipsychotic dosing. Journal of Clinical Psychiatry *61*: 344–348

Woods S W (2003) Chlorpromazine equivalent doses for the newer atypical antipsychotics. Journal of Clinical Psychiatry *64*: 663–667

Woods S W, Sullivan M C, Neuse E C, Diaz E, Baker C B, Madonick S H, Griffith E E, Steiner (2003) Racial and ethnic effects on antipsychotic prescribing practices in a community mental health center. Psychiatric Services *54*: 177–179

Yorston G, Pinney A (2000) Chlorpromazine equivalents and percentage of British National Formulary maximum recommended dose in patients receiving high-dose antipsychotics. Psychiatric Bulletin *24*: 130–132

APPENDIX 7 DATA COLLECTION FORM, ETHNICITY STUDY 2

Name data collector ……. **Ethnicity of data collector** …….

Patient interview * = confirmed with nurse ** = confirm with case note

Patient's Initials	**Date of data collection**	**NHS Number or hospital number if no NHS number**	**Ward Name**	**Gender** (Male or Female)	**Do you smoke tobacco?*** (Smoker = S or Non-Smoker = NS)	**When not in hospital are you currently working?** **(Employed = E; Unemployed = UE; Retired = R; student S*)*	**Education When did you leave school? Did you do further study after school?**** (primary, secondary, 6th form or degree level)	**Language** Of the languages you speak which one do you speak most fluently/easily?

Patient interview (continued) * = confirmed with nurse ** = confirm with case notes

Patient's initials (continued from page 1)	**What is your ethnic origin e.g. white British?** ***(self ascribed)***	**Parental ethnic origin**		**Did you have a choice of antipsychotic medication to take? (Y/N)****	**Did you receive any written or verbal information about your antipsychotic medication? (Y/N)****	**History of or current substance abuse** (Yes/No)**	**Weight (in kg)**	**Height (in cm)**
		Mother e.g. white British	**Father e.g. black African**					

Case notes and information from health care professionals

Patient's initials (continued from page 1)	Age (years)	Significant physical illness	Forensic history current or previous Y/N	Race/ethnicity of prescriber of antipsychotic on current drug chart	Race/ethnicity of patient's Consultant	Clinical Global Impression Rating (from SHO or named nurse – see attached scale)

Clinical Global Impression

Severity of Illness Considering your total clinical experience with this particular population, what is the severity of illness of this patient now?
0 = Not assessed
1 = Normal, not ill at all
2 = Borderline mentally ill
3 = Mildly ill
4 = Moderately ill
5 – Markedly ill
6 = Severely ill
7 = Among the most severely ill patients

Case notes information * = confirmed with nurse

Patient's initials (continued from page 1)	**Current diagnosis (ICD 10 coding)**	**Current Mental Health Act section (e.g. 2,3,37,41 etc)**	**Duration of illness (in years and months)**	**Number of <u>previous</u> admissions (0,1, 2-5 or >5)**	**Length of current admission (to day of data collection) (days)**	**History of or current non-compliance Yes/No***

Current Antipsychotic Therapy. Count regular (including depot) and prn. For 'prn' record amount given in last full day, if none drug dose is 0%. *If more than 3 antipsychotics, add together all maxima and put in brackets the number of antipsychotics prescribed.* For risperidone po use 6mg as maximum dose. AP = antipsychotic. If prn po/im haloperidol or olanzapine write po and im as separate AP.

Patient's initials (from page 1)	**Antipsychotic 1**			**Antipsychotic 2**			**Antipsychotic 3**			**Total dose as % max** (add 1+2+3 %)	**On regular anti-cholinergic? (Yes/No)**
	Drug name	**Total AP daily dose and route (mg/day po or depot dose/week)**	**Drug dose (% max)**	**Drug name**	**Total AP daily dose and route (mg/day po or depot dose/week)**	**Drug dose (% max)**	**Drug name**	**Total AP daily dose and route (mg/day po or depot dose/week)**	**Drug dose (% max)**		

Case notes and medication chart information

Patient's initials (from page 1)	Length of current antipsychotic treatment in days (for AP administered)			Previous treatment with <u>any of current regular</u> antipsychotic medication (Yes/No)	Previous antipsychotic treatment (name all antipsychotics received)	<u>Current</u> all other regular drug therapy (Give list)
	Antipsychotic 1	Antipsychotic 2	Antipsychotic 3			

APPENDIX 8 PROCEDURE, ETHNICITY STUDY 2

Research procedure
Antipsychotic prescribing in black and white patients

1. Call wards before data collection to check is convenient to visit for the audit.
2. Print off list of patients on acute adult ward (including PICUs) that you are visiting (if you have computerised lists).
3. Check ethnicity of the patients on the ward on the electronic notes system or in patients' notes (usually on clerking form). Patients who are black (African or Caribbean descent) or white (NOT mixed or Asian) **can** be included in the study. You will need to check what codes your trust uses for ethnicity – usually Office of National Statistics ones – I have provided a print out.
4. Go through drug charts on ward and write list of patients who are prescribed and are receiving a regular antipsychotic.
5. You now have your list of patients to approach i.e. those who are black or white **and** on a regular antipsychotic.
6. Ask nurses to highlight who on your list is safe to approach.
7. Ask nurse to introduce you to each patient 1 at a time.
8. Explain to each patient what study is about e.g. 'we are doing a study to make sure that medicines are used fairly for black and white patients. I need to ask you a few questions about you and your ethnic origin, weigh and measure how tall you are. This should take about 5 minutes. Would this be ok with you?'
9. For those who do not want to take part in the study record the following information from notes on the sheet provided:
   - Persons initials
   - NHS number
   - Ward
   - Sex
   - Age
   - Ethnic origin

   Patients who are asleep or off the ward are not classed as 'refusers'.
10. Ask patient questions from the data collection form about
    - Smoking status
    - Employment – e.g. when you are not in hospital are you currently working?
    - Education – e.g. when did you leave school? Did you go on to further study?
    - First language – e.g. what languages do you speak – which is your 'best'/most fluent one?
    - Ethnic origin – e.g. what would you describe your ethnicity as?
    - Parental origin – e.g. and your parents were they both white British/black African etc.? If parents' ethnicity is white and black then patient is excluded as they are classed as mixed.
    - Choice of antipsychotic – e.g. did you have a choice of your antipsychotic treatment?
    - Information – e.g. did you get any written (e.g. a leaflet) or did anyone discuss the good and not so good things about your antipsychotic treatment?
    - Substance misuse – e.g. do you use or have you used street drugs or excess alcohol now or in the past?

11. Measure height and weight. Use cm and kg. Use the treatment room for the data collection as the height and weighing scales are there. If no height measurer then use a mark on the wall and tape measure. Some patients like to know their weight in stones too, switch on back of scales to change to stones. Get patient to take their shoes off for accurate measurement.
12. Ask named nurse or SHO for CGI-S as on questionnaire.
13. Collect rest of information for the data collection form from notes
    - Significant physical illness e.g. heart disease, asthma - if unsure record
    - Forensic history – currently charged with an offence or a history of conviction for an offence
    - Race/ethnicity of prescriber (on current chart and consultant – use same classification as used for patients). If you can't find out from staff or prescriber medical staffing will have this information.
    - Current diagnosis – if no ICD-10 code then write current diagnosis (may be more than 1)
    - Current Mental Health Act section
    - Mean percentage maximum dose = daily dose ÷ maximum daily dose of drug x 100 to get % (or for depots – weekly dose of depot ÷ maximum weekly dose of depot x 100 to get %).
    - Easiest to get previous antipsychotic treatments from Part 1 and 2 summaries but you will need old notes for patients who have been ill for decades.
    - If you are not sure about anything then please call Anne on 07905315371

- **It is very important to fill in the whole table with information. If the entire table is not completed we cannot use that patient's data.**

- Sections that can take time to find full data on include: previous antipsychotics, number of previous admissions, length of illness – may need old notes or good part 1 summary for these sections.

APPENDIX 9 ANTIPSYCHOTICS AND ETHNICITY STUDY 2

BJPsych | The British Journal of Psychiatry (2008) 193, 161–162. doi: 10.1192/bjp.bp.108.050427

Short report

Ethnicity and quality of antipsychotic prescribing among in-patients in south London

Anne Connolly and David Taylor

Summary
Ethnicity may influence treatment decisions in mental disorders. We undertook a survey of the prescribing of antipsychotics for in-patients in three south London mental health trusts. A total of 255 patients (152 White, 103 Black) were included. Median dose of antipsychotic (% of licensed dose) was 58.3% for White and 50.0% for Black patients (adjusted effect size=0.14, 95% CI –0.34 to 0.63). High-dose antipsychotics were prescribed to 15.1% of White and 11.7% of Black patients (adjusted odds ratio (OR)=0.5, 95% CI 0.19–1.33), and antipsychotic polypharmacy was recorded for 25.7% and 31.1% respectively (adjusted OR=3.05, 95% CI 1.44–6.46). Prescribing quality was similar for Black and White patients.

Declaration of interest
None. Funding detailed in Acknowledgements.

There have been suggestions of institutional racism in UK mental health services.[1] Several, mainly American, studies indicate that Black patients are more likely than White patients to receive high doses of antipsychotics and depot formulations[2–4] and less likely to be treated with atypical antipsychotics.[5] Many of the studies are limited by the failure to collect and correct for other factors likely to affect prescribing practice. We published a single-centre study[6] of antipsychotic prescribing which took into account over 20 potentially confounding factors, but found no difference in corrected odds of receiving high doses of antipsychotics or antipsychotic polypharmacy. We wanted to know whether our results would differ in a larger study with greater power to detect smaller differences and which included participants from other trusts.

Method

This study was conducted at the South London and Maudsley, South West London and St George's, and Oxleas National Health Service (NHS) Trusts during late 2006 and early 2007. We sought and obtained individual approvals for the study through local clinical audit channels.

Patients included were in-patients, designated Black or White, and prescribed and taking one or more regular antipsychotics. Patients were classed as Black if both parents were also Black (that is, Africans, African Americans and African–Caribbeans). Mixed-race patients were excluded. All suitable patients on all acute general psychiatry wards in every hospital within each trust were approached over a 3-month period in 2006/2007: none was excluded except for the reason above. The outcomes of dose (expressed as a percentage of licensed maximum),[7] being prescribed antipsychotic medication above maximum dose, polypharmacy and costs were determined by reference to each patient's medication chart and to standard reference texts for dose[8] and cost.[9]

Potential confounding factors (23 in total) were predetermined and details were obtained from case notes, self-report, or by measurement or calculation and confirmed by nursing or medical staff where appropriate. Clinical Global Impression–Severity[10] (CGI–S) was rated on the day of data collection (nurse or medical staff assessment).

A sample size of 298 was calculated to be required to give an 80% chance of detecting a 5% absolute difference for our main outcome (dose) (α=0.05, ρ=0.8). We aimed to compare four outcomes (dose, rate of polypharmacy, high-dose prescribing and use of atypical antipsychotics) between our two groups and to adjust comparisons for the effect of confounding (predictive) variables. For the outcome of dose we used a linear regression model to provide an estimate of unadjusted effect of ethnicity on dose. Potential confounding variables were then tested to identify predictive factors (significance level of $P<0.1$). Predictive factors were then included in a rerun regression model, producing adjusted effect size for ethnicity. Transformations were used when necessary. A similar approach was used for the binary outcomes of high dose, polypharmacy and prescribing of atypical drugs, but with logistic regression modelling used.

Results

We approached 300 patients and 255 gave informal informed consent to be interviewed. Of the 45 patients who declined to take part, 21 (46.7%) were Black, 23 (51.1%) were male and the mean age was 41.7 years. Details of included patients are given in the online Table DS1.

Median dose was 58.3% for White patients and 50.0% for Black patients (adjusted effect size=0.14, 95% CI –0.34 to 0.63; P=0.56). High-dose antipsychotics (>100% licensed maximum) were prescribed to 15.1% of White and 11.7% of Black patients (adjusted OR=0.5, 95% CI 0.19–1.33; P=0.16) and polypharmacy to 25.7% and 31.1% respectively (adjusted OR=3.05, 95% CI 1.44–6.46; P=0.004). With polypharmacy, the adjusted odds ratio was largely driven by centre differences: one centre showed an exceptionally high rate of polypharmacy in Black patients (74% *v.* 37% in White patients; other centres: 13% *v.* 17% and 16% *v.* 10% respectively). There was no difference in the prescribing of atypical antipsychotics (White 77.6%, Black 68.9%: adjusted OR=0.57, 95% CI 0.21–1.5; P=0.25).

Discussion

In this study, ethnicity was not significantly associated with dose of antipsychotic, the prescribing of high-dose antipsychotics or the use of atypical antipsychotics. Prescribing quality was thus no worse for Black patients than for White patients. Only the outcome of adjusted odds ratio for antipsychotic polypharmacy showed any association with ethnicity. This is an important observation but it should be noted that absolute rates of polypharmacy differed markedly in only one centre and the overall difference in prevalence was small (25.7% for White *v.* 31.1% for Black patients).

Our findings are therefore in some contrast to studies which suggest a higher likelihood of higher-dose prescribing in Black patients[2–5] and a lower use of atypical drugs.[5] This may reflect true differences in practice at different times (there is evidence of ethnic differences in prescribing in the 1990s in south London)[11] or in different locations (many of the studies[3–5] examine US prescribing) but may also be linked to the relatively limited extent of adjustment for confounding variables in previous studies. Adjustment for these confounders is essential to the process of establishing or otherwise ethnicity as having an association with prescribing quality.

There were several limitations in our study design. We did not meet our recruitment target of 298 patients, although confidence intervals ultimately excluded major differences in outcome, particularly with respect to a possibility of a lower quality of prescribing for Black people. In addition, some of our data collection relied on patient self-report – a notoriously unreliable source, especially, perhaps, in psychiatric in-patients. Also, our assessment of clinic status was approximate (using the CGI–S scale) and may not of have been relevant to patients' condition at the time of the initial prescription. Lastly, our sample was exclusively in-patients and so our results may not generalise to the majority of patients now treated in the community.

Notwithstanding these limitations, it is reasonable to conclude that in this study prescribing quality did not differ substantially between Black and White patients. Black patients were not prescribed higher doses than White patients. Black patients are more likely to receive antipsychotic polypharmacy, but this difference was only noticeably higher in one centre. Black patients were just as likely as White patients to receive atypical antipsychotics.

Anne Connolly, MRPharmS, Pharmacy Department, Maudsley Hospital, London; **David Taylor**, PhD, Pharmacy Department, Maudsley Hospital, and School of Biomedical Sciences, King's College, London, UK

Correspondence: David Taylor, Pharmacy Department, Maudsley Hospital, Denmark Hill, London SE5 8AZ, UK. Email: David.Taylor@slam.nhs.uk

First received 9 Nov 2007, final revision 28 Jan 2008, accepted 21 Apr 2008

Acknowledgements

We thank Andrew Fuller, Deirdre McArdle, Laraine James, Sarah Jones and Vanessa Jones for data collection, and Sabine Landau and Manoharan Andiappan for statistical analysis. This study was funded by Trustees of the South London and Maudsley NHS Foundation Trust.

References

1 Norfolk, Suffolk and Cambridgeshire Strategic Health Authority. *Independent Inquiry into the Death of David Bennett*. NSCSHA, 2003 (http://nscsha.org.uk/resources/pdf/review_inquiry/david_bennett_inquiry/david_bennett_inquiry_report_2003.pdf).

2 Segal SP, Bola JR, Watson MA. Race, quality of care, and antipsychotic prescribing practices in psychiatric emergency services. *Psychiatr Serv* 1996; **47**: 282–6.

3 Walkup JT, McAlpine DD, Olfson M, Labay LE, Boyer C, Hansell S. Patients with schizophrenia at risk for excessive antipsychotic dosing. *J Clin Psychiatry* 2000; **61**: 344–8.

4 Diaz FJ, de Leon J. Excessive antipsychotic dosing in 2 U.S. State hospitals. *J Clin Psychiatry* 2002; **63**: 998–1003.

5 Kuno E, Rothbard AB. Racial disparities in antipsychotic prescription patterns for patients with schizophrenia. *Am J Psychiatry* 2002; **159**: 567–72.

6 Connolly A, Rogers P, Taylor D. Antipsychotic prescribing quality and ethnicity: a study of hospitalized patients in south east London. *J Psychopharmacol* 2007; **21**: 191–7.

7 Yorston G, Pinney A. Chlorpromazine equivalents and percentage of *British National Formulary* maximum recommended dose in patients receiving high-dose antipsychotics. *Psychiatr Bull* 2000; **24**: 130–2.

8 British Medical Association & Royal Pharmaceutical Society of Great Britain. *British National Formulary No 51*. BMJ Publishing Group, 2007.

9 Healthcare Republic. *Monthly Index of Medical Specialties*. Haymarket Medical Publications, 2007.

10 Guy W. The Clinical Global Impressions Scale. In *ECDEU Assessment Manual for Psychopharmacology (rev. edn)* (ed W Guy): 157–69. National Institute of Mental Health, 1976.

11 Lloyd K, Moodley P. Psychotropic medication and ethnicity: an inpatient survey. *Soc Psychiatry Psychiatr Epidemiol* 1992; **27**: 95–101.

EXTRA CONTENT ONLINE

APPENDIX 10 DATA COLLECTION DEFINITIONS, ETHNICITY STUDY 3

Inclusion Screening

Regular antipsychotic	Patients prescribed at least one regular (or when required 'prn' dose received in last 24 hours) oral or injectable antipsychotic on a medication chart	Medication chart

Included Subjects

Data Title	Data Definition	Location of data
Age	On date of data collection	Notes
Ethnicity	As 2001 ONS Census (see below) i.e. white or mixed or Asian/Asian British or black/black British or Chinese or other (state what)	Notes
Employment	Employed = working when not in hospital Unemployed = not working when not in hospital Retired Student	Notes, nursing staff
Education	Record highest completed – primary; secondary; A level/6th form college; degree level	Notes, nursing staff
First Language	Language spoken at home	Notes, nursing staff
Smoking status	**Current** cigarette smoker i.e. smoker or non smoker	Notes, nursing staff
Substance Misuse	Excessive **current** use of street drugs and/or alcohol	Notes, nursing staff
Weight	Use kilograms.	Notes or nurse to measure
Significant physical illness	Major physical disease e.g. heart disease, asthma, diabetes - if unsure record	Notes
Primary diagnosis (ICD-10 codes)	F00-F09 organic, including symptomatic, mental disorders e.g. dementia F10-F19 mental and behavioural disorders because of psychoactive substance use F20-F29 schizophrenia, schizotypal and delusional disorders F30-F39 mood (affective) disorders e.g. bipolar affective disorder, recurrent depressive disorder F40-F48 neurotic, stress related and somatoform disorders e.g. agoraphobia, panic disorder F50-F59 behavioural syndrome associated with physiological disturbance and physical factors e.g. anorexia F60-F69 disorders of adult personality and behaviour e.g. paranoid personality disorder	Notes

	F70-F79 mental retardation F80-F89 disorders of psychological development F90-F98 behavioural and emotional disorders with onset during/occurring in childhood/adolescence F99 unspecified mental disorder Not known - the clinical team has not yet reached a diagnosis	
Forensic history	**Currently** charged with an offence or a **history** of conviction for an offence	Notes
Ethnicity of patient's consultant	Use same classification as used for patients i.e. Office for National Statistics (ONS) 2001 Census definitions below Medical staffing will have this information	Consultant or medical staffing department
Current Mental Health Act section?	Record if Sectioned (any type) or Informal	Notes, nursing staff
Duration of illness	Time since 1st contact with psychiatric services In days, years or months depending duration	Notes
Number of previous admissions	To inpatient or home treatment care Categorised into 0, 1, 2-5 or >5	Notes
Length of current inpatient admission	Time in days of inpatient admission (not just on current ward as they may have moved) to day of data collection	Notes or nursing staff (if patient only been on 1 ward)
History of or current non-compliance with medication	Known history of or current non-compliance with medication e.g. previous relapse because of non-compliance	Notes and medication chart
Current regular antipsychotic treatment	Count regular (including depot) and prn. For 'prn' record amount given in last full day, if none drug dose is 0%. If more than 5 antipsychotics, add together all maxima and put in brackets the number of antipsychotics prescribed. **If written prn PO/IM write PO (oral) and IM (intramuscular) as separate antipsychotics**. **Record even if prn dose is 0%**	Medicine chart

Mean percentage (%) maximum dose	(Current daily dose ÷ maximum daily dose of drug) x 100 = % Depots (weekly dose of depot ÷ maximum weekly dose of depot) x 100 = %	Medicine chart and maximum doses chart
Regular anticholinergic?	Benzatropine, orphenadrine, procyclidine, trihexyphenidyl (i.e. benzhexol)	Medicine chart
Length of current antipsychotic treatment	In days, applies to **main (highest percentage dose)** antipsychotic treatment Look at previous (not only current) chart(s)	Medicines chart(s) or notes if long-term treatment
Previous treatment with any of current regular antipsychotic(s)	Has the patient taken any of their regular current antipsychotic treatments before for previous episodes of illness?	Notes
Previous antipsychotic treatments	Names of antipsychotics had previously	Notes
Current all other regular drug therapy	As written on current drug chart(s)	Medicine chart

Office of National Statistics 2001 Ethnicity Codes

White
British
Irish
Any other white background

Mixed
White and black Caribbean
White and black African
White and Asian
Any other mixed background

Asian or Asian British
Indian
Pakistani
Bangladeshi
Any other Asian background

Black or black British
Caribbean
African
Any other black background

Chinese or other ethnic group
Chinese
Any other ethnic group

APPENDIX 11 ANTIPSYCHOTIC NAMES AND DOSES

Generic name	Brand name(s)	Maximum dose (daily dose for oral and weekly dose for IM)
Amisulpride	Solian	1200mg
Aripiprazole	Abilfy tablets and injection	Tablets or aqueous injection = 30mg
Benperidol	Anquil	1.5mg
Chlorpromazine	Largactil	1000mg
Clozapine	Clozaril, Denzapine, Zaponex	900mg
Flupentixol (or flupenthixol) tablets or decanoate depot injection	Depixol	Tablets = 18mg Depot injection = 400mg per week
Fluphenazine tablets or decanoate depot injection	Moditen - tablets Modecate – depot injection	Tablets = 20mg Depot injection = 50mg per week
Haloperidol tablets and decanoate depot injection	Dozic - oral liquid Haldol - depot and aqueous injection Serenace – tablets/capsules	Tablet/liquid = 30mg Aqueous injection = 18mg Depot injection = 75mg per week
Levomepromazine (or methotrimeprazine)	Nozinan	1000mg
Olanzapine	Zyprexa tablets and velotabs, injection	Tablets and injection 20mg
Pericyazine	Neulactil	300mg
Perphenazine	Fentazin	24mg
Pimozide	Orap	20mg
Pipotiazine (pipothiazine) palmitate	Piportil	Injection 50mg per week
Promazine	No branded product	800mg
Quetiapine (doses depend on indication)	**Seroquel**	**750mg = psychosis or schizophrenia** **800mg = bipolar disorder**
Risperidone	Risperdal – tablets, quicklets; Risperdal Consta – long-acting injection	Tablets = 16mg Injection = 25mg weekly (50mg 2 weekly)
Sertindole	Serdolect	24mg
Sulpiride	Dolmatil, Sulpitil, Sulpor	2400mg
Trifluoperazine	Stelazine	50mg
Zotepine	Zoleptil	300mg

Zuclopentixol (or zuclopenthixol)	Clopixol Depot and Clopixol Accuphase	Tablets = 150mg Decanoate depot injection = 600mg/week Acetate intramuscular injection (Accuphase) (not depot) = 400mg

Drugs now discontinued	
Generic	**Brand Name**
Droperidol	Dropleptan
Remoxipride	Roxiam
Thioridazine	Melleril

APPENDIX 12 DATA COLLECTION FORM, ETHNICITY STUDY 3

Name of data collector……

Each patient's information is collected in 1 vertical column. See data collection definitions for full explanation.

	1	2	3
Patient's Initials			
Date of data collection			
NHS Number (or hospital number if no NHS number)			
Ward Name			
Gender (male or female)			
Age (years)			
Ethnicity white or mixed or Asian/Asian British or black/black British or Chinese or other (state what)			
Employment status (Employed = E; Unemployed = UE; Retired = R; student S)			
Education (Primary or Secondary or A level/6th form college or Degree level)			
First language			
Smoking status (Smoker = S or Non-Smoker = NS)			
Substance Misuse? (Yes/No)			
Weight (kg)			
Significant physical illness (list all)			

	1	2	3
Primary diagnosis (ICD code)			
Forensic history (Yes/No)			
Race/ethnicity of patient's Consultant (coded as 2001 ONS Census)			
Current Mental Health Act section? (sectioned or informal)			
Duration of illness (In days or years or months)			
Number of <u>previous</u> admissions (0 or 1 or 2-5 or >5)			
Length of current inpatient admission (to day of data collection) (days)			
History of or current non-compliance Yes/No			
Drug name			
Antipsychotic number 1 – total daily dose (mg/day po or depot dose/week)			
Route (oral or intramuscular)			
Drug dose as % maximum			

	1	2	3
Drug name			
Antipsychotic number 2 – total daily dose (mg/day po or depot dose/week)			
Route (oral or intramuscular)			
Drug dose as % maximum			
Drug name			
Antipsychotic number 3 – total daily dose (mg/day po or depot dose/week)			
Route (oral or intramuscular)			
Drug dose as % maximum			
Drug name			
Antipsychotic number 4 – total daily dose (mg/day po or depot dose/week)			
Route (oral or intramuscular)			
Drug dose as % maximum			

	1	2	3
Drug name			
Antipsychotic number 5 – total daily dose (mg/day po or depot dose/week)			
Route (oral or intramuscular)			
Drug dose as % maximum			
Total dose as % maximum (Add % maximum of antipsychotic numbers 1+2+3+4+5)			
On regular anti-cholinergic? (Yes/No			
Length of current antipsychotic treatment in days (for highest % max dose antipsychotic administered)			
Previous treatment with <u>any of current regular</u> antipsychotic medication (Yes/No)			
Previous antipsychotic treatments (Name all antipsychotics received)			
<u>Current</u> all other regular drug therapy (Give list)			

Contact details for any questions - Anne Connolly 0790 531 5371 or 020 3228 2317

APPENDIX 13 HEALTH CARE COMMISSION BME GROUP DISTRIBUTION

Number of patients by trust and percentages Count Me In Census 2007
Healthcare Commission, Mental Health Act Commission, National Institute for Mental Health England

	Organisation name	NHS/ PVH	England/ Wales	Black or black British + mixed - white and black Caribbean/African	Grand Total
1	South London And Maudsley NHS Trust	NHS	England	399	990
2	West London Mental Health NHS Trust	NHS	England	259	875
3	East London and The City Mental Health NHS Trust	NHS	England	234	637
4	Barnet, Enfield and Haringey Mental Health NHS Trust	NHS	England	193	693
5	Central and North West London Mental Health NHS Trust	NHS	England	189	780
6	Birmingham and Solihull Mental Health NHS Trust	NHS	England	147	783
7	South West London and St George's Mental Health NHS Trust	NHS	England	117	645
8	Nottinghamshire Healthcare NHS Trust	NHS	England	111	940
9	Camden And Islington Mental Health and Social Care Trust	NHS	England	101	373
10	Oxleas NHS Foundation Trust	NHS	England	75	450
11	North East London Mental Health NHS Trust	NHS	England	62	404
12	Mersey Care NHS Trust	NHS	England	57	633
13	Manchester Mental Health and Social Care Trust	NHS	England	51	269
14	Avon and Wiltshire Mental Health Partnership Trust	NHS	England	45	679
15	Bolton, Salford and Trafford Mental Health Services	NHS	England	39	570
16	Oxfordshire and Buckinghamshire Mental Health Partnership NHS Trust	NHS	England	37	458
17	Leicestershire Partnership NHS Trust	NHS	England	26	433
18	Kneesworth House Hospital	PVH	England	23	99
19	Leeds Mental Health Teaching NHS Trust	NHS	England	22	365
20	Hampshire Partnership NHS Trust	NHS	England	18	655

Categories included

Black or black British	Caribbean
Black or black British	African
Black or black British	Any other black background
Mixed	White and black Caribbean
Mixed	White and black African

Original Paper

Psychopharm

Journal of Psychopharmacology
25(5) 704–709

DOI: 10.1177/0269881109387841
jop.sagepub.com
SAGE

Antipsychotic prescribing in Black and White hospitalised patients

Anne Connolly[1], David Taylor[1], Anna Sparshatt[1] and Victoria Cornelius[2]

Abstract

Ethnicity may affect the prescribing of antipsychotic treatment. Previous UK studies conducted in south London have found few differences in antipsychotic prescribing quality for Black and White patients. This larger multicentre study examined the effect of ethnicity on antipsychotic prescribing quality in areas serving the largest proportions of Black patients in the UK. A cross-sectional survey with collection of multiple confounding factors potentially affecting outcomes in eight secondary care units in England over a three month period. Participants were Black or White inpatients prescribed regular antipsychotics on the day of the survey. Antipsychotic dose (expressed as a percentage of licensed maximum), high dose (being prescribed antipsychotic medication above maximum dose), polypharmacy (more than one antipsychotic prescribed), type (typical or atypical antipsychotic) and costs were the main outcome measures. Data were collected for 938 patients. There were no significant differences in any outcome by ethnicity: dose (adjusted percentage difference 0.97 [95% confidence interval (CI) −4.28, 6.22], $p = 0.72$); high dose (adjusted odds ratio (AOR) 0.98 [CI 0.63, 1.51], $p = 0.92$); polypharmacy *prescribed* (AOR 1.15 [CI 0.87, 1.51], $p = 0.33$); polypharmacy *administered* (AOR 1.08 [CI 0.78, 1.49], $p = 0.66$); use of typical antipsychotics (AOR 1.25 [CI 0.87, 1.79], $p = 0.22$); and cost (adjusted effect size 1.75 [CI −9.81, 13.31], $p = 0.77$). Antipsychotic prescribing practice did not differ between Black and White patients.

Keywords

Antipsychotics, ethnicity, prescribing

Introduction

Black patients are more likely to be hospitalised and detained in UK psychiatric hospitals compared with their White counterparts (Singh et al., 2007; Tyrer et al., 2006). Prescribing of antipsychotics may also be affected by ethnicity. Differences in dose, (Diaz and de Leon, 2002; Segal et al., 1996; Walkup et al., 2000) type (Kreyenbuhl et al., 2003; Kuno and Rothbard, 2002) and number (Taylor, 2004) of antipsychotics prescribed have been described, predominantly in American studies. These findings have resulted in accusations of institutional racism in mental health services (Norfolk, 2003). Previously we have examined the effect of ethnicity on the prescribing of antipsychotics in the UK both in our trust (National Health Service (NHS) provider of secondary care mental health services) (Connolly et al., 2007) and more recently in our neighbouring mental health trusts (Connolly and Taylor, 2008). Neither study revealed major differences in the quality of antipsychotic prescribing but statistical power was somewhat limited, few inpatient units were studied and the geographical area under investigation was restricted to south London. The undertaking of larger pharmacoepidemiological (e.g. computer database) studies is precluded by the need to collect data on and correct for numerous potential confounders of prescribing practice. This extent of data collection is best undertaken in inpatient units where data can be readily and accurately recorded. In the present study our aim was to examine the influence of ethnicity (specifically being Black or White) on antipsychotic prescribing practice in inpatient units serving populations with the largest proportions of Black people in the UK.

Method

Ten mental health trusts were approached to take part in the study. These trusts were chosen because they were serving populations with the largest proportions of Black patients in the UK (Healthcare Commission, 2007). Nine trusts agreed to take part and eight, (Barnet, Enfield & Harringey (BEH), Camden & Islington (C&I), Central & North West London (CNWL), East London & City (ELC), Manchester Mental Health & Social Care Trust (Manchester), North East

[1]Pharmacy Department, Maudsley Hospital, London, UK.
[2]Nutrition and Respiratory Biomedical Research Units, Southampton General Hospital, UK.

Corresponding author:
Anne Connolly, Pharmacy Department, Maudsley Hospital, Denmark Hill, London SE5 8AZ, UK
Email: anne.connolly@slam.nhs.uk

London (NEL), Nottinghamshire Healthcare (Nottingham), and South London & Maudsley (SLaM)), completed the data collection during late 2008 and early 2009. We sought and obtained individual trust approvals for the study through local clinical audit channels. All data were anonymised at source and participants were not identifiable by the data analyst (Anne Connolly [AC]).

The main outcomes of the study were dose (expressed as a percentage of licensed maximum [Yorston and Pinney, 2000]), being prescribed antipsychotic medication above maximum British National Formulary (BNF) dose (British Medical Association and Royal Pharmaceutical Society of Great Britain, 2008), polypharmacy (more than one antipsychotic prescribed), type of antipsychotic (typical or atypical antipsychotic) and costs. These were determined by reference to each patient's medication chart and to standard reference texts for dose (BNF) and cost (MIMS, 2008).

Subjects

Patients included were all adult inpatients on acute general psychiatry wards, designated Black or White, and were prescribed and taking one or more regular antipsychotics on the day of the data collection (or had received a when-required 'p.r.n.'(*pro re nata*) dose in the last 24 hours). Recording of ethnicity is mandatory for all inpatients and patients were classed as Black (Black British, Black African, Black Caribbean, Black other) or White (White British, White Irish, White other) according to their medical notes (as categorised by the Office for National Statistics) (Office for National Statistics, 2001). Mixed race patients were excluded in this analysis. All suitable patients on acute general psychiatry wards within each trust were included over a three month period in 2008/2009: none was excluded except for reasons above.

Data collection

Data were collected by pharmacists or doctors working within each trust. Each data collector was trained by one of the authors (AC). Potential confounders were predetermined and the following were determined by reference to casenotes: age; current legal status; current substance misuse; diagnosis; duration of illness; education; employment status; forensic history (previous conviction or currently charged with an offence); gender; history of or current non-compliance; language; length of current admission; number of previous admissions; previous antipsychotic treatments; previous treatment with current antipsychotic medication; race of patient's consultant; smoking status; weight. The remaining confounders i.e. anticholinergic prescribed regularly, length of current antipsychotic treatment and route of administration were collected from prescription charts.

Statistical analysis

Justification for sample size. We performed a 'power' calculation before starting the study. A sample size of 788 was calculated to be required to have an 80% chance of detecting a 5% (55% vs 50%) absolute difference for our main outcome (percentage maximum dose) between Black and White patients (assuming a standard deviation of 25)

Data analysis. We aimed to compare the five outcomes between our two groups (Black and White patients) and to adjust the resulting comparisons for the effect of confounding variables. Centre was not included as a confounder in the data analysis but we did examine whether or not prescribing practice varied by centre. Data collection forms were checked for accuracy and completeness three times before entry onto a database. In addition, the database was again checked against paper records after all the data had been entered.

Baseline demographic and clinical characteristics were analysed by ethnicity. The null hypothesis was that Black patients were prescribed the same total median dose of antipsychotics as White patients. A linear regression model was then used to investigate whether there was a difference between Black and White patients for the continuous outcomes of dose and cost of treatment. Confounding variables to be included in the model were selected using a stepwise forward selection procedure with a selection criterion of 10% and removal criterion of 20%. Where the relationship between continuous potential confounding variables and the outcomes could not be assumed to be linear (a requirement for regression modelling) and transforming variables did not induce a linear relationship, restricted cubic splines were applied. The fit of each model and the influence of observations were examined. This modelling produced an adjusted effect size (i.e. median percentage difference for dose and median cost difference) for ethnicity for the outcomes of dose and cost. A similar approach was used for the binary outcomes of high dose, polypharmacy and prescribing of typical drugs, but using logistic regression modelling. This modelling allowed the calculation of adjusted odds ratios (AORs). Identification of confounding variables was as described above. The fit of each model was examined using residual analysis.

Initially a complete case analysis was performed for each of the regression models i.e. where only patients with complete covariate data were included in the model. However, excluding patients without full information may result in biased estimates. Consequently, values were imputed for patients with missing covariate data using a multiple imputation method. For each variable an appropriate regression model was specified. Five datasets containing imputed values were created then each data set was analysed and the relevant parameters were averaged across the data to give a single estimate. The analysis was performed using the function ICE in Stata version 10. The adjusted results reported are for the imputed data sets.

Results

We collected data on 938 patients from eight centres of which 541 (57.7%) were White and 397 (42.3%) Black. SLaM provided 199 (21.2%) subjects, CNWL 148 (15.8%), ELC 121 (12.9%), BEH 109 (11.6%), C&I 98 (10.4%), NEL 94 (10%), Manchester 89 (9.5%), and Nottingham 80 (8.5%). Demographic and clinical characteristics of these patients

Table 1. Demographic and clinical categories by ethnicity

Variable (*n*)	White *n* = 541 (%)	Black *n* = 397 (%)
Centre (938)		
SLaM	88 (44.2)	111 (55.8)
CNWL	91 (61.5)	57 (38.5)
ELC	45 (37.2)	76 (62.8)
BEH	51 (46.8)	58 (53.2)
C&I	59 (60.2)	39 (39.8)
NEL	68 (72.3)	26 (27.7)
Manchester	73 (82)	16 (18)
Nottingham	66 (82.5)	14 (17.5)
Gender (938)		
Male	323 (59.7)	267 (67.3)
Female	218 (40.3)	130 (32.7)
Employment (921)		
Unemployed	475 (90.5)	360 (90.9)
Employed	22 (4.2)	18 (4.5)
Student	5 (0.9)	16 (4)
Retired	23 (4.4)	2 (0.5)
Education (858)		
Primary	67 (13.9)	48 (12.7)
Secondary	276 (57.3)	205 (54.1)
6th form/to 18 years	95 (19.7)	91 (24)
University	44 (9.1)	35 (9.2)
Language (916)		
Not English	41 (7.9)	48 (12.2)
English	481 (92.1)	346 (87.8)
Smoking status (896)		
Smoker	389 (76.9)	265 (67.9)
Non-smoker	117 (23.1)	125 (32.1)
Diagnosis (875)		
Schizophrenia	314 (64.3)	306 (79.1)
Other	174 (35.7)	81 (20.9)
Race of Consultant (912)		
White	358 (67.5)	254 (66.5)
Mixed	6 (1.1)	4 (1)
Asian	75 (14.2)	45 (11.8)
Black	60 (11.3)	56 (14.7)
Chinese/other	31 (5.8)	23 (6)
Previous treatment with current antipsychotic (841)		
Yes	292 (62.4)	248 (66.5)
Mental Health Act Status (934)		
Informal	199 (37.1)	92 (23.2)
Sectioned (compulsorily detained in hospital)	338 (62.9)	305 (76.8)
Forensic History (863)		
Yes	179 (37.1)	191 (50.1)
Previous antipsychotics (812)		
None	92 (20.5)	86 (23.6)
1	116 (25.9)	71 (19.5)
2 to 5	203 (45.3)	181 (49.7)
≥6	37 (8.3)	26 (7.1)
Previous admissions (871)		
None	46 (9.5)	48 (12.4)
1	48 (9.9)	44 (11.3)
2 to 5	172 (35.6)	151 (38.9)
≥6	217 (44.9)	145 (37.4)
Non-compliance history (874)		
Yes	373 (76.1)	322 (83.9)
Route (938)		
Oral	432 (79.9)	280 (70.5)
Intramuscular	109 (20.1)	117 (29.5)
Regular anticholinergic use (918)		
Yes	86 (16.3)	65 (16.6)
Substance misuse (892)		
Yes	216 (43)	188 (48.2)

Table 2. Continuous demographic and clinical categories by ethnicity

Variable (*n* = complete)	White (*n* = 541)	Black (*n* = 397)
Median **age** in years (95% CI), *n* = 938	42 (40, 43)	35 (33, 37)
Median **duration of illness** in days (95% CI), *n* = 840	3950 (3387, 4380)	2920 (2190, 3285)
Median **weight** in kilograms (95% CI), *n* = 833	77 (75, 79)	80 (78, 83)
Median **length of admission** in days (95% CI), *n* = 926	57 (49, 62)	58 (50, 67)
Median **length of treatment with current antipsychotic** in days (95% CI), *n* = 831	40 (31, 46)	40 (35, 51)

CI: confidence interval

by ethnicity and centre are described in Tables 1 and 2. Not all confounder data were available for all subjects at the time of the survey. The proportion of complete confounder data was 94.6% (18,627 complete data points) and outcome data 100%; missing data were imputed as described. Each outcome model was adjusted for multiple confounders.

Outcomes are described in Figures 1–6. There were no significant differences in any outcome by ethnicity.

Discussion

Main findings

In this multicentre study of antipsychotic prescribing practice in Black and White patients we found no significant differences in dose, high dose, polypharmacy, or type and cost of treatment, after adjustment for multiple confounding factors. Our study included a large number of patients from different parts of the UK. The numerous associations found between potential confounders and outcomes confirm the necessity for adjustment of these factors.

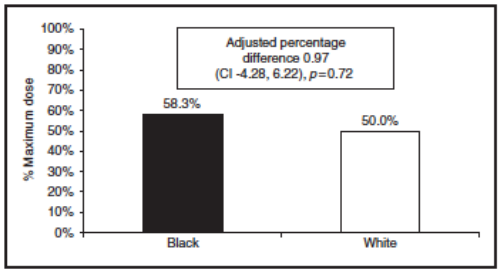


Figure 1. Median dose*. Unadjusted percentage difference 2.28 (CI −3.04, 7.61) $p = 0.4$.

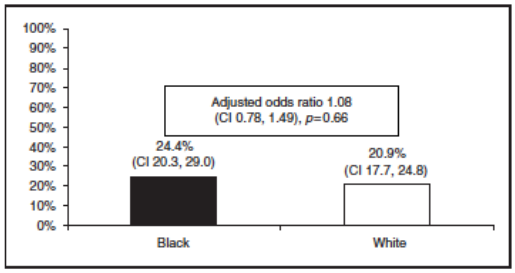


Figure 4. Proportion for whom polypharmacy *administered*. Unadjusted odds ratio 1.22 (CI 0.9, 1.67), $p = 0.2$.

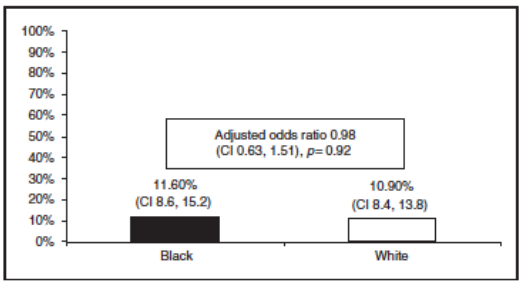


Figure 2. Proportion receiving high dose (>100% maximum dose). Unadjusted odds ratio 1.07 (CI 0.71, 1.61), $p = 0.74$.

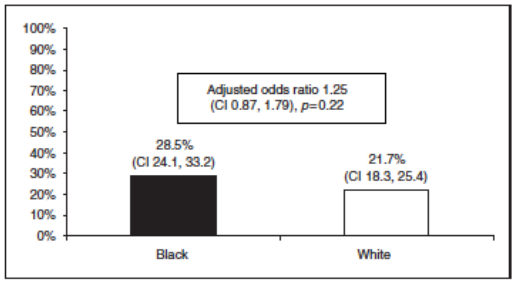


Figure 5. Proportion prescribed a typical antipsychotic. Unadjusted odds ratio 1.44 (CI 1.06, 1.94), $p = 0.02$.

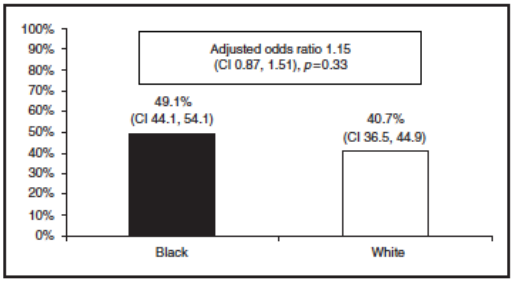


Figure 3. Proportion for whom polypharmacy *prescribed*. Unadjusted odds ratio 1.41 (CI 1.08, 1.83), $p = 0.01$.

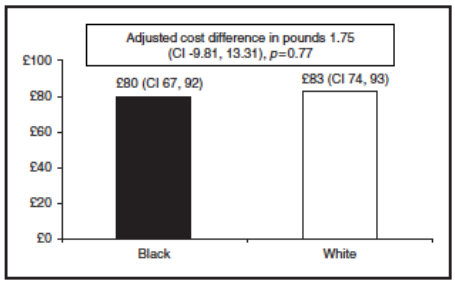


Figure 6. Median cost of antipsychotic treatment. Unadjusted cost difference in pounds 1.08 (CI −10.6, 12.8), $p = 0.86$.

Comparison with previous studies

Most of the studies examining antipsychotic use by ethnicity have been completed in the US. Differences in antipsychotic treatment in Black and White patients included; a greater likelihood of receiving an antipsychotic (Delbello et al., 2000; Flaskerud and Hu, 1992; Szarek and Goethe, 2003), higher doses (Diaz and de Leon, 2002; Segal et al., 1996; Walkup et al., 2000), older drugs (Daumit et al., 2003; Fleck et al., 2002) and more frequent use of depot formulations (Arnold et al., 2004; Kuno and Rothbard, 2002). These studies adjusted, unlike the present study, for only a

few confounding factors affecting the prescribing of antipsychotics. Outcomes from these studies may not be comparable with ours because of differences in design and other factors related to healthcare settings and practices in different countries at different times.

There are few UK studies examining ethnicity and antipsychotic use. One survey (Lloyd and Moodley, 1992) found no significant differences (after adjustment for five confounding variables) in doses of antipsychotics taken by Black and White patients. However Black patients were more likely than White to be receiving a depot and at a significantly higher dose. Other UK studies, which were not designed to specifically examine prescribing by ethnicity, have not found an effect of race on antipsychotic high-dose use (Paton et al., 2008) and polypharmacy (Lelliott et al., 2002). Our recent cross-sectional survey of antipsychotic prescribing quality and ethnicity included several hundred patients from three NHS mental health trusts and again accounted for multiple confounding factors (Connolly et al., 2007; Connolly and Taylor, 2008). Overall these surveys found few differences between Black and White patients for the same outcomes we have used in this study although higher costs of antipsychotic medication and polypharmacy were significantly more likely in Black patients.

Limitations

Limitations of our study include the cross-sectional design (which allows examination of prescribing practice only at a single time point) and the inability to obtain data on confounding factors for all patients. Also we recruited centres for this study by approaching mental health trusts containing the largest populations of Black and minority ethnic group patients. These centres, because of their ethnically diverse patient population, may be in some way more or less likely to demonstrate prejudicial prescribing in an environment of multicultural tolerance and prescriber diversity (Goldacre et al., 2004). Nonetheless, in our previous study (Connolly and Taylor, 2008) we included one centre that had a predominantly White population and found no differences in antipsychotic prescribing quality between centres. We did not include centre as a potential confounder in this study because we considered variation in prescribing by centre to be an outcome rather than a confounder. A separate analysis including centre as a confounder did not alter our results. Finally, confidence intervals around some outcome measures were wider than anticipated. This was a result of larger than expected variances and because of the number of confounding variables identified and accounted for.

Conclusions

There have long been concerns expressed by patients, carers (Department of Health, 2003; South London and Maudsley NHS Trust, 2005) and the UK government (Norfolk, 2003) about differences in the prescribing of antipsychotics by race. Our study addresses these concerns and our findings suggest that across eight NHS trusts the quality of prescribing of antipsychotics is not substantially different for Black and White patients.

Acknowledgement

All authors had full access to all of the data in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis.

Funding

This work was supported by a research grant awarded by Delivering Race Equality (DRE) in Mental Healthcare Programme, part of the Mental Health Equalities Programme in the National Mental Health Development Unit. The DRE did not contribute to the design, data collection, analysis or interpretation, writing or submission for publication.

Conflict of interest statement

None

References

Arnold LM, Strakowski SM, Schwiers ML, et al. (2004) Sex, ethnicity, and antipsychotic medication use in patients with psychosis. *Schizophr Res* 66(2–3): 169–175.

British Medical Association and Royal Pharmaceutical Society of Great Britain (2008) *British National Formulary*. 56th edition. London: BMJ Group and RPS Publishing.

Connolly A, Rogers P and Taylor D (2007) Antipsychotic prescribing quality and ethnicity: a study of hospitalised patients in south east London. *J Psychopharmacol* 21(2): 191–197.

Connolly A and Taylor D (2008) Ethnicity and quality of antipsychotic prescribing among in-patients in south London. *Br J Psychiatry* 193(2): 161–162.

Daumit GL, Crum RM, Guallar E, et al. (2003) Outpatient prescriptions for atypical antipsychotics for African Americans, Hispanics, and whites in the United States. *Arch Gen Psychiatry* 60(2): 121–128.

Delbello MP, Soutullo CA and Strakowski SM (2000) Racial differences in treatment of adolescents with bipolar disorder. *Am J Psychiatry* 157(5): 837–838.

Department of Health. (2003) *Inside Outside: Improving mental health services for black and minority ethnic communities in England*. Available at: http://www.dh.gov.uk/

Diaz FJ and de Leon J (2002) Excessive antipsychotic dosing in 2 U.S. State hospitals. *J Clin Psychiatry* 63(11): 998–1003.

Flaskerud JH and Hu LT (1992) Racial/ethnic identity and amount and type of psychiatric treatment. *Am J Psychiatry* 149(3): 379–384.

Fleck DE, Hendricks WL, Delbello MP and Strakowski SM (2002) Differential prescription of maintenance antipsychotics to African American and white patients with new-onset bipolar disorder. *J Clin Psychiatry* 63(8): 658–664.

Goldacre MJ, Davidson JM and Lambert TW (2004) Country of training and ethnic origin of UK doctors: database and survey studies. *BMJ* 329(7466): 597.

Healthcare Commission. (2007) *Count me in* 2007. *Results of the* 2007 *national census of inpatients in mental health and learning disability services in England and Wales*. Available at: http://www.wales.nhs.uk/

Kreyenbuhl J, Zito JM, Buchanan RW, Soeken KL and Lehman AF (2003) Racial disparity in the pharmacological management of schizophrenia. *Schizophr Bull* 29(2): 183–194.

Kuno E and Rothbard AB (2002) Racial disparities in antipsychotic prescription patterns for patients with schizophrenia. *Am J Psychiatry* 159(4): 567–572.

Lelliott P, Paton C, Harrington M, Konsolaki M, Sensky T and Okocha C (2002) The influence of patient variables on

polypharmacy and combined high dose of antipsychotic drugs prescribed for in-patients. *Psychiatr Bull* 26: 411–414.

Lloyd K and Moodley P (1992) Psychotropic medication and ethnicity: an inpatient survey. *Soc Psychiatry Psychiatr Epidemiol* 27(2): 95–101.

Monthly Index of Medical Specialities (MIMS) (December 2008) London: Haymarket Medical Media.

Norfolk SaCSHA. (2003) *Independent Inquiry into the death of David Bennett*. Available at: http://www.nscsha.nhs.uk/resources/pdf/review_inquiry/david_bennett_inquiry/david_bennett_inquiry_report_2003.pdf. 2003.

Office for National Statistics. (2001) *Census 2001 – Ethnicity and Religion in England and Wales*. Available at: http://www.statistics.gov.uk/

Paton C, Barnes TR, Cavanagh MR, Taylor D and Lelliott P (2008) High-dose and combination antipsychotic prescribing in acute adult wards in the UK: the challenges posed by p.r.n. prescribing. *Br J Psychiatry* 192: 435–439.

Segal SP, Bola JR and Watson MA (1996) Race, quality of care, and antipsychotic prescribing practices in psychiatric emergency services. *Psychiatr Serv* 47(3): 282–286.

Singh SP, Greenwood N, White S and Churchill R (2007) Ethnicity and the Mental Health Act 1983. *Br J Psychiatry* 191(2): 99–105.

South London and Maudsley NHS Trust. (2005) *Race Equality Scheme and Action Plan 2005–2008*. Available at: http://sites.intranet.slam.nhs.uk/

Szarek BL and Goethe JW (2003) Racial differences in use of antipsychotics among patients with bipolar disorder. *J Clin Psychiatry* 64(5): 614–615.

Taylor DM (2004) Prescribing of clozapine and olanzapine: dosage, polypharmacy and patient ethnicity. *Psychiatr Bull* 28(7): 241–243.

Tyrer P, Suryanarayan G, Rao B, et al. (2006) The bed requirement inventory: a simple measure to estimate the need for a psychiatric bed. *Int J Soc Psychiatry* 52(3): 267–277.

Walkup JT, McAlpine DD, Olfson M, Labay LE, Boyer C and Hansell S (2000) Patients with schizophrenia at risk for excessive antipsychotic dosing. *J Clin Psychiatry* 61(5): 344–348.

Yorston G and Pinney A (2000) Chlorpromazine equivalents and percentage of British National Formulary maximum recommended dose in patients receiving high-dose antipsychotics. *PsychiatrBull* 24(4): 130–132.

APPENDIX 15 FACTORS ASSOCIATED WITH NON EVIDENCE-BASED PRESCRIBING OF ANTIPSYCHOTICS

Therapeutic Advances in Psychopharmacology *Original Research*

Factors associated with non evidence-based prescribing of antipsychotics

Ther Adv Psychopharmacol
2014, Vol. 4(6) 247–256
DOI: 10.1177/2045125314540298

Anne Connolly and David Taylor

Abstract

Objectives: Non evidence-based prescribing of antipsychotics is common in the UK and internationally with high doses and polypharmacy the norm. These practices often remain even after systematic attempts are made to change. We aimed to establish which factors are linked to antipsychotic prescribing quality so we can identify and target patients for interventions to improve quality and allow us to understand further the drivers of non evidence-based prescribing.

Method: A cross-sectional survey with a collection of factors potentially affecting antipsychotic prescribing quality outcomes was carried out in eight secondary care units in England. Participants were inpatients prescribed regular antipsychotics on the day of the survey. Antipsychotic dose, polypharmacy, type and route were the main outcome measures.

Results: Data were collected for 1198 patients. Higher total dose was associated with greater weight, higher number of previous admissions, longer length of admission, noncompliance with medication and use of an atypical antipsychotic. A lower total dose was associated with clozapine use. Polypharmacy was associated with not being a patient at the South London and Maudsley NHS Trust centre, the subject having a forensic history, a greater number of previous admissions and higher total dose. Younger age, not being detained under a Mental Health Act section, atypical antipsychotic use and oral route were predictors of antipsychotic monotherapy. Atypical antipsychotic use was associated with oral route, higher total dose, being administered only one antipsychotic, having had fewer previous antipsychotics and no anticholinergic use. Use of the oral route was associated with not being sectioned under the Mental Health Act, atypical antipsychotic use, younger age, non-schizophrenia diagnosis, fewer previous admissions and a lower total dose.

Conclusion: In patients with chronic illness who are detained, heavier, noncompliant, not taking clozapine and on a depot antipsychotic, prescribers use larger doses and antipsychotic polypharmacy. We found that use of percentage of licensed maximum doses favours typical antipsychotics arbitrarily, and that high doses and polypharmacy are inextricably linked.

Keywords: antipsychotic agents, ethnology, drug administration routes, clozapine, polypharmacy, inappropriate prescribing

Introduction

Non evidence-based prescribing of antipsychotics is common in the UK and internationally (Barnes and Paton, 2011]. Most studies examining outcomes such as dose, type, route and antipsychotic combination report a situation where high doses and polypharmacy are the norm [Harrington *et al.* 2002; Taylor *et al.* 2002]. These practices often remain even after systematic and vigorous attempts are made to change [Paton *et al.* 2008]. Although individual organisations can make dramatic improvements in prescribing quality through multidisciplinary quality improvement programmes [Mace and Taylor, 2014], such successes are rare.

Antipsychotic polypharmacy should be avoided for several reasons. Firstly it is illogical. Combining medicines with different mechanisms of action has understandable theory for the treatment of conditions such as hypertension [NICE, 2011]. However, antipsychotics have broadly similar

Correspondence to:
David Taylor, BSc, MSc, PhD, FRPharmS
Pharmacy Department, Maudsley Hospital, London SE5 8AZ, UK
David.Taylor@slam.nhs.uk
Anne Connolly
Pharmacy Department, Maudsley Hospital, London, UK

mechanisms of action [Kapur and Seeman, 2001] and clinically meaningful differences between them (with the exception of clozapine) are small [Leucht *et al.* 2013]. In addition, using depot and oral medication together negates the very reason for prescribing a long-acting formulation. Secondly combining antipsychotics is harmful. We know movement, metabolic, cardiac and neurocognitive adverse effects are more likely with combinations [Waddington *et al.* 1998; Carnahan *et al.* 2006; Correll *et al.* 2007; Elie *et al.* 2010] as is increased mortality [Joukamaa *et al.* 2006]. Thirdly polypharmacy is financially costly. Prescribing more than one antipsychotic obviously costs more, particularly for atypical combinations, and increases risk of nonadherence [Fenton *et al.* 1997]. Furthermore polypharmacy is a major risk factor for high dose prescribing which compounds all of these harms.

What makes these prescribing practices so obdurate despite robust evidence to suggest they are both harmful and illogical? Most of the studies in this area reveal a lack of response to a single antipsychotic agent as the main reason for prescribing combinations. Other reasons include the use of 'when required' antipsychotics, attempting to treat persistent aggression and trying to avoid high dose monotherapy (that is, prescribing two drugs within their licensed dose range is seen as better than one drug at supramaximal dose). However, polypharmacy and high doses of antipsychotics are prescribing practices that are inextricably linked as one commonly leads to the other. Changing these practices is difficult with multifaceted interventions often providing only modest improvements [Thompson *et al.* 2008; Constantine *et al.* 2010].

Of course there are some instances when combined antipsychotic prescribing is evidence-based. These include cross titration of antipsychotics during switching [Taylor, 1997], clozapine augmentation to improve efficacy [Taylor and Smith, 2009], managing side effects (e.g. adding aripiprazole to combat raised prolactin or metabolic symptoms [Shim *et al.* 2007; Henderson *et al.* 2009]) and rapid tranquillisation [Taylor *et al.* 2012].

We previously examined antipsychotic prescribing quality [Connolly *et al.* 2010] in black and white patients in hospitals serving the largest proportions of minority ethnic groups in the UK. Initially we adjusted prescribing outcomes for multiple confounding factors to determine if prescribing differed by ethnicity. In the current investigation we aimed to establish which factors are linked to antipsychotic prescribing quality. This will help us to identify which patients may be at risk of non evidence-based prescribing, enable us to target them for interventions to improve quality, and allow us to understand further the drivers of such prescribing.

Method

This study was conducted in eight mental health trusts in London, Nottingham and Manchester and is a new analysis of a previously reported investigation. The details of the method of this study are described extensively elsewhere [Connolly *et al.* 2010].

Briefly data were collected for all adult inpatients on acute psychiatric wards in the trusts taking part in the study. Subjects were of all ethnicities, i.e. Black, White, Asian, Mixed or Other (as categorised by the most recent UK Office for National Statistics Census 2001 at the time of data collection), and were prescribed and taking one or more regular antipsychotics. Outcomes in our initial study were total dose, type of antipsychotic, polypharmacy (both prescribed and administered), high dose [that is, more than 100% of British National formulary (BNF) dose] and cost. This analysis examines predictors of the first three outcomes listed in addition to route of administration and clozapine use. These new outcomes were derived from the current dataset and have previously been reported to be influenced by ethnicity [Lloyd and Moodley, 1992; Kuno and Rothbard, 2002; Whiskey *et al.* 2011].

Data were collected by medical and pharmacy staff at each trust and numerous confounding factors were collected from case notes: age; legal status; substance misuse; diagnosis; duration of illness; education; employment status; forensic history; gender; compliance history; language; length of current admission; number of previous admissions; patient ethnicity; previous antipsychotic treatments; previous treatment with current antipsychotic; race of patients consultant; smoking status; and weight. Other factors were collected from prescription charts including anticholinergic prescribed, clozapine use, dose, length of treatment with current antipsychotic, polypharmacy prescribed, polypharmacy administered, type of antipsychotic and route of administration.

Statistical analysis

The relationship between patient and clinical variables listed earlier and each of our five outcomes was assessed using multivariate linear regression for the continuous outcome of total dose and multivariate binary logistic regression for the remaining categorical outcomes. Initially, previous research studies examining associations between antipsychotic prescribing and race were evaluated to determine which variables were important to include in our model, i.e. which variables predicted or adjusted outcomes. In addition each variable was entered into a simple univariate regression model to determine the strength of the relationship between predictor and outcome. All variables with a significance of $p < 0.05$ were then included in a multivariate regression model using a backward method [likelihood ratio (LR) for logistic method, entry $p < 0.05$, removal $p < 0.1$] with a complete cases dataset. Where patient ethnicity was not significantly associated with outcome it was included in the model as it is the predictor of interest in our study. Finally significant variables from this method were included in each model using the enter method. Non-significant variables were removed singly in order of least significance until a final parsimonious model was determined.

Data were checked for outliers using descriptive statistics and graphical boxplot representation. Two-way interactions between variables included in the model were tested for association. No interactions were significantly associated with our outcomes and did not improve model fit. Full diagnostics were performed including testing assumptions of linear and logistic regression, model fit and residuals. Log transformation of continuous predictor total dose ensured assumption of linearity between continuous variables and total dose. Effects of missing data on model fit were performed. All analyses were conducted using IBM SPSS statistics version 21.

Results

Study population

Demographic and patient variable details for the total sample are listed in Tables 1 and 2. Data were collected for a total of 1198 patients. Around a quarter of patients had at least one unrecorded demographic detail. Effects of missing data for each outcome showed no significant effects on model fit.

Causes of associations with log total dose

Log transformation of total dose ensured residuals homoscedasticity and normality. Associations with higher log total dose (Table 3) were greater weight, higher number of previous admissions, longer length of admission, noncompliance with medication and use of an atypical antipsychotic. The taking of clozapine was associated with a lower log total dose.

Causes of associations with clozapine use

No significant predictors of taking clozapine were identified from analysis of this dataset.

Causes of associations with polypharmacy prescribed

Associations with being prescribed more than one antipsychotic (Table 4) were; not being a patient of the South London and Maudsley (SLaM) NHS Trust centre, the subject having a forensic history and a higher total dose. Younger age, not being detained under a mental health act section and oral route were predictors of prescribed antipsychotic monotherapy.

Causes of associations with polypharmacy administered

The effects of overdispersion in the model were reduced by using the dispersion parameter to rescale standard errors and confidence intervals. Associations with being administered more than one antipsychotic (Table 5) were greater number of previous admissions and higher total dose. Atypical antipsychotic use predicted being administered monotherapy.

Causes of associations with type of antipsychotic

Associations with atypical antipsychotic use (Table 6) were; oral route, higher total dose, being administered only one antipsychotic, having had fewer previous antipsychotics and no anticholinergic use.

Causes of associations with route of administration

Associations with oral route (Table 7) were not being Sectioned under the Mental Health Act, atypical antipsychotic use, younger age, non-schizophrenia diagnosis, fewer previous admissions and a lower total dose.

Table 1. Demographic and clinical variables.

Variable		*n* (%)	Missing (%)
Missing data (all variables)	Complete cases	866 (72.3)	332 (27.7)
Centre	SLaM	228 (19)	0 (0)
	Not SLaM	970 (81)	
Gender	Female	427 (35.6)	0 (0)
	Male	771 (64.4)	
Patient ethnicity	White	562 (46.9)	17 (1.4)
	Black	410 (34.2)	
	Other	209 (17.4)	
Employment	Not employed	1127 (94.1)	22 (1.8)
	Employed	49 (4.1)	
Education	Secondary	618 (51.6)	105 (8.8)
	Other	475 (39.6)	
Language	Not English	168 (14)	34 (2.8)
	English	996 (83.1)	
Smoking status	Nonsmoker	325 (27.1)	55 (4.6)
	Smoker	818 (68.3)	
Substance misuse	No	628 (52.4)	57 (4.8)
	Yes	513 (42.8)	
Diagnosis	Not schizophrenia	329 (27.5)	76 (6.3)
	Schizophrenia	793 (66.2)	
Forensic history	No	636 (53.1)	87 (7.3)
	Yes	475 (39.6)	
Race of consultant	White	768 (64.1)	45 (3.8)
	Not white	385 (32.1)	
Section status	Sectioned	824 (68.8)	6 (0.5)
	Informal	368 (30.7)	
Previous admissions	0 or 1	254 (21.2)	83 (6.9)
	2 or more	861 (71.9)	
Noncompliant history	No	227 (18.9)	77 (6.4)
	Yes	894 (74.6)	
Clozapine use	No	1074 (89.6)	0 (0)
	Yes	124 (10.4)	
Route of administration	Intramuscular	280 (23.4)	0 (0)
	Oral	918 (76.6)	
Type of antipsychotic	Typical	284 (23.7)	0 (0)
	Atypical	914 (76.3)	
Polypharmacy prescribed	No	640 (53.4)	1 (0.1)
	Yes	557 (46.5)	
Polypharmacy administered	No	911 (76)	29 (2.4)
	Yes	258 (21.5)	
Anticholinergic use	No	963 (80.4)	41 (3.4)
	Yes	194 (16.2)	
Previous treatment with current antipsychotic	No	382 (31.9)	138 (11.5)
	Yes	678 (56.6)	
Previous number of antipsychotic treatments	0 or 1	468 (39.1)	178 (14.9)
	2 or more	552 (46.1)	

SLaM, South London and Maudsley NHS Trust.

Discussion

Main findings

What factors affect our prescribing? The associations of our outcomes reveal important insights into antipsychotic prescribing quality. As we found in our previous publications, race was not a predictor of any outcome [Connolly *et al.* 2010].

Higher doses were prescribed to patients of greater weight, those not compliant with medication, those on atypical antipsychotics, with

Table 2. Continuous demographic and clinical variables.

Variable	Median	Missing (%)
Median age (years; range)	38 (18–76)	2 (0.2)
Median weight (kg; range)	77.8 (33–175.7)	156 (13)
Median length of admission (days; range)	56 (1–4210)	31 (2.6)
Median duration of illness (days; range)	3285 (1–18250)	131 (10.9)
Median total dose (% maxima; range)	55.5 (2.5–272.5)	41 (3.4)

Table 3. Multivariate linear regression model for log total dose outcome.

Variables	Coefficient B	Standard error	*p*-value	95% CI for B	
				Lower bound	Upper bound
Constant	0.95	0.41	0.021	0.15	1.76
Weight (log)	0.45	0.09	0.001	0.26	0.63
Previous admissions	0.30	0.06	0.001	0.19	0.42
Length of admission (log)	0.10	0.02	0.001	0.06	0.13
Compliance history	0.19	0.06	0.001	0.08	0.30
Clozapine use	−0.35	0.08	0.001	-0.50	-0.20
Type of antipsychotic	0.44	0.05	0.001	0.34	0.55

n = 978.
R^2 = 0.153.
Reference categories: previous admissions = ≤1; compliant = yes; clozapine use = no; type of antipsychotic = typical.
CI, confidence interval.

Table 4. Multivariate logistic regression model for polypharmacy prescribed.

Variables	Coefficient B	Standard error	*p*-value	Odds ratio	95% CI for odds ratio	
					Lower	Upper
Constant	−0.87	0.33	0.008	0.42	N/A	N/A
Centre	0.80	0.17	0.001	2.23	1.60	3.11
Age	−0.02	0.01	0.001	0.98	0.97	0.99
Forensic history	0.34	0.14	0.015	1.40	1.07	1.84
Section status	−0.42	0.15	0.005	0.66	0.49	0.88
Route of administration	−0.40	0.16	0.012	0.67	0.49	0.92
Total dose	0.02	0.002	0.001	1.02	1.01	1.02

n = 1071.
-2 Log likelihood = 1306.144.
Reference categories for predictors; centre = SLaM; forensic history = no; section status = sectioned; route of administration = intramuscular.
CI, confidence interval; N/A, not applicable.

a longer length of admission and a greater number of previous admissions. Weight and dose were probably associated both because antipsychotics cause weight gain [Rummel-Kluge *et al.* 2010] and perhaps because prescribers use higher doses for bigger people. Those non-compliant with medication were also prescribed higher doses probably because dose is often increased when effect is lost through covert noncompliance. In addition noncompliance increases the likelihood of relapse and relapse is associated with overall dose increases [Wyatt, 1991; Harrington *et al.* 2002].

Table 5. Multivariate logistic regression model for polypharmacy administered.

Variable	Coefficient B	Standard error	*p*-value	Odds ratio	95% CI of odds ratio	
					Lower	Upper
Constant	−3.68	0.32	0.001	0.03	N/A	N/A
Previous admissions	0.59	0.78	0.02	1.78	0.39	8.27
Type of antipsychotic	−1.07	0.62	0.001	0.34	0.10	1.15
Total dose	0.04	0.01	0.001	1.03	1.02	1.05

n = 1081.
-2 Log likelihood = 833.632.
Reference categories for predictors; previous admission = ≤1; type of antipsychotic = typical.
CI, confidence interval; N/A, not applicable.

Table 6. Multivariate logistic regression model for atypical type of antipsychotic.

Variables	Coefficient B	Standard error	*p*-value	Odds ratio	95% CI for odds ratio	
					Lower	Upper
Constant	−1.27	0.26	0.001	0.28	N/A	N/A
Route	2.64	0.20	0.001	14.08	9.51	20.83
Polypharmacy administered	−0.89	0.24	0.001	0.41	0.26	0.66
Previous number of antipsychotics	−0.55	0.18	0.003	0.58	0.40	0.83
Anticholinergic use	−1.42	0.23	0.001	0.24	0.16	0.38
Total dose	0.02	0.003	0.001	1.02	1.02	1.03

n= 996.
-2 Log likelihood = 798.936.
Reference categories predictors; route = intramuscular; polypharmacy administered = no; previous number of antipsychotics = ≤1; anticholinergic use = no.
CI, confidence interval; N/A, not applicable.

Table 7. Multivariate logistic regression model for oral route of administration.

Variables	Coefficient B	Standard error	*p*-value	Odds ratio	95% CI for odds ratio	
					Lower	Upper
Constant	1.80	0.41	0.001	6.06	N/A	N/A
Age	−0.02	0.01	0.022	0.98	0.97	0.99
Diagnosis	−0.99	0.22	0.001	0.37	0.24	0.57
Section status	0.64	0.21	0.002	1.90	1.26	2.86
Previous admissions	−0.75	0.26	0.004	0.47	0.28	0.79
Type of antipsychotic	2.57	0.19	0.001	13.09	9.08	18.86
Total dose	−0.007	0.002	0.001	0.99	0.98	0.99

n= 1070.
-2 Log likelihood = 862.526.
Reference categories for predictors; diagnosis = not schizophrenia; section status = sectioned; previous admission = ≤1; type of antipsychotics = typical.
CI, confidence interval; N/A, not applicable.

The association of atypical antipsychotic use with higher doses was unexpected. However, recommended doses of typical antipsychotics are usually a much lower proportion of their maximum dose than atypicals. This is because efficacious dopamine blockade occurs at much lower doses of typical antipsychotics than was previously understood [Kapur *et al.* 2000]. For example,

haloperidol 6 mg/day gives near maximal dopamine receptor blockade for antipsychotic effect but the UK maximum dose at the time of the study was 30 mg/day (and was previously 200 mg/day).The effective dose of olanzapine is probably around 13 mg/day [Bishara *et al.* 2013]. Thus an effective dose of haloperidol is 20% of the licensed maximum but for olanzapine it is 65%. Longer length of admission and a greater number of previous admissions are proxy measures of severity and chronicity of illness, and so their association with higher doses is understandable. These associations demonstrate the practice of increasing the dose at relapse and admission. Interestingly, clozapine use predicted a lower total dose perhaps reflecting a lower risk of polypharmacy because of the greater efficacy with this unique antipsychotic [Kane *et al.* 1988]. It was not possible to fit a model for clozapine use to determine this assumption.

Antipsychotic polypharmacy was associated with higher total doses, greater number of previous admissions, having a forensic history and not being a patient at the SLaM centre. Monotherapy was predicted by younger age, not being detained under a Mental Health Act Section, oral route of administration and use of an atypical antipsychotic. Antipsychotic polypharmacy and higher doses are inextricably linked [Harrington *et al.* 2002] and their association in our data reflects current UK prescribing practice [Paton *et al.* 2008]. Once again a chronic illness course indicated by a greater number of previous admissions was associated with non evidence-based prescribing, this time with polypharmacy. As with high dose, polypharmacy is more likely in those with many previous episodes as their illness is likely to be more severe and intractable. Patients with a forensic history have often been prescribed high doses and more than one antipsychotic [Lelliott *et al.* 2002], particularly depot plus oral combinations [Barnes *et al.* 2009]. Reasons for this are unclear but prescribers suggest lack of efficacy of monotherapy as a key factor [Haw and Stubbs, 2003; Grech and Taylor, 2012].The influence of centre on polypharmacy was robust. The NHS trusts other than SLaM had a greater preponderance for prescribing of more than one antipsychotic.Whilst changing polypharmacy prescribing practice is difficult, the SLaM centre has individually reported marked improvements in combination and high-dose prescribing through the use of a quality improvement programme, thus explaining this association [Mace and Taylor, 2014]. Previous studies of antipsychotic prescribing have found that polypharmacy does differ by centre [Connolly and Taylor, 2008] indicating perhaps that the culture of an organisation has a powerful effect on prescribing patterns [Barnes and Paton, 2011].

Younger age is associated with fewer previous episodes of illness and a greater sensitivity to some adverse effects of antipsychotics. This is reflected in the association of youth with antipsychotic monotherapy. Similarly not being detained suggests a less severe illness presentation and a lower risk of polypharmacy. Overall we can see that high doses and polypharmacy are more common in severe and chronic subjects. This probably reflects a need by prescribers to 'do something' rather than adherence to any evidence base. Encouragingly, atypical use was also associated with antipsychotic monotherapy, perhaps finally reflecting changes in recommended prescribing practice for the newer antipsychotics [Paton *et al.* 2008].

Atypical antipsychotic use was associated with patients on oral medication, antipsychotic monotherapy, having had fewer previous antipsychotics and not taking anticholinergic medication. Higher doses were also associated with atypical antipsychotic use (as they were when dose was our outcome) possibly because, as discussed earlier, atypicals have much narrower ranges of licensed doses than typicals, we used percentage maximum to measure dose and older antipsychotics can be difficult to tolerate at high doses. For example, the maximum licensed dose of flupentixol decanoate is 32 times greater than the minimum dose whilst for risperidone injection it is only twice as high. Both atypical antipsychotic use and oral route were associated with each other when used as outcome and predictor and to a similar large magnitude. This provides reassurance of our methodological processes. Atypical antipsychotics are, when used at recommended doses, less likely to cause movement side effects than older agents and so would not require anticholinergic medication to treat extrapyramidal effects. Given that atypical antipsychotics are predominantly available as only oral formulations, the robust association of these two factors is clearly explained.

Use of the oral route was associated with younger age, not having a diagnosis of schizophrenia, informal Section status, fewer previous admissions, atypical antipsychotic use and a lower dose.

Again younger age, informal Section status and fewer previous admissions suggest a less severe and earlier stage of illness and a reduced use of depot antipsychotics. As discussed earlier, atypical antipsychotics were mostly only available as oral formulations and so accounts for this association. The association between oral route and low dose may be due to doses of depots. This is because the maximum doses of depots have not reduced in line with recommended doses (e.g. flupentixol depot UK maximum dose of 400 mg/week; usual recommended dose 30 mg/week). Diagnosis was associated with oral doses being used in patients without schizophrenia. Antipsychotics used for other conditions, for example bipolar disorder, are often only available as oral formulations and may not be prescribed long term as depot antipsychotics commonly are in schizophrenia [Barnes *et al.* 2009].

Comparison with previous studies

Previous analysis of our dataset used multiple imputations for missing data, black and white patients data only, did not include our outcomes as covariates, and used total dose outcome complete cases only (the primary outcome in our initial study).

Predictors of antipsychotic polypharmacy include anticholinergic use, male gender, poor symptom control and longer lengths of admission to hospital [Barnes and Paton, 2011]. Again these may be markers of a chronic illness course.

Can our study be generalised to a larger population? Other larger studies [Paton *et al.* 2008; Barnes *et al.* 2009] examining combination antipsychotic prescribing found similar results in patients with broadly comparable demographic data. For example, diagnosis of schizophrenia was 61% in one of these studies [Paton *et al.* 2008] and 66.2% in our sample. Within sample centre diagnoses were also largely similar.

What can we do about non evidence-based prescribing? Intensive quality improvement programmes can help and for some individual units progress may be dramatic. For the most part, however, these interventions result in, at best, modest change. Prescribers do not want to prescribe in a non evidence-based manner; they are audited, compared with their peers and NHS trusts take these data seriously, particularly when ranked against other trusts. The main reason prescribers state for polypharmacy and high dose prescribing is poor response to current treatment. This is because of the limited range of effective drugs for treating schizophrenia. Clozapine is well known to be the most efficacious antipsychotic; however, it is often underused because of side effects and patient reluctance to receive the blood testing monitoring requirements [Gee *et al.* 2013]. We know that there are long delays from when patients should start clozapine (after lack of response or tolerability to two antipsychotic trials) to when they actually do [Howes *et al.* 2012] and we know prescribers would prefer to use combinations rather than prescribe clozapine [Neilsen *et al.* 2010]. Methods to encourage use of clozapine for patents whose symptoms are refractory to treatment are effective [Gee *et al.* 2013]. We need to educate prescribers and encourage patients to use clozapine, otherwise the inefficacy and adverse effects of non evidence-based prescribing are likely to remain.

Limitations

The predictive power of our linear and logistic regression models was poor and the magnitude of effects was small overall. This is despite (or possibly because of) the collection of a large number of variables that could affect prescribing of antipsychotics which adds to our model's statistical complexity. Unfortunately we did not collect data on patients' mental state (a predictor in other studies of antipsychotic use and race [Van Dorn *et al.* 2005; Shi *et al.* 2007] nor the reasons why clinicians prescribed on a non evidenced-based manner, so making it difficult to judge the appropriateness of any individual prescription. The low predictive ability of our models suggests that other factors as yet unknown are also major predictors of our prescribing quality. In addition using complete cases may have affected our results, although previous analyses of this data including missing data [Connolly *et al.* 2010] produced models with similar predictive power.

Conclusion

In patients with chronic illness who are detained, heavier, noncompliant, not taking clozapine and on a depot antipsychotic, prescribers use larger doses and antipsychotic polypharmacy. We found that use of percentage maximum doses favours typical antipsychotics arbitrarily and that high doses and polypharmacy are inextricably linked. In addition poor compliance may lead to

erroneous dose increases. Newer agents were used for patients who had been treated with fewer previous antipsychotics and not taking anticholinergic medicines. Oral medicines were used for patients who were younger, not detained, did not have schizophrenia, had had fewer previous admissions, on atypical antipsychotics and taking a lower dose. Race did not play a part in prescribing quality decisions.

Acknowledgements

The authors wish to thank Olubanke Dzahini for her statistical support and advice.

Funding

This work was funded by the Delivering Race Equality (DRE) in Mental Healthcare Programme, part of the Equality and Human Rights Commission.

Conflict of interest statement

The authors declare no conflicts of interest in preparing this article.

References

Barnes, T. and Paton, C. (2011) Antipsychotic polypharmacy in schizophrenia. *CNS Drugs* 25: 383–399.

Barnes, T., Shingleton-Smith, A. and Paton, C. (2009) Antipsychotic long-acting injections: prescribing practice in the UK. *Br J Psychiat* 195: S37–S42.

Bishara, D., Olofinjana, O., Sparshatt, A., Kapur, S., Taylor, D. and Patel, M. (2013) Olanzapine: a systematic review and meta-regression of the relationships between dose, plasma concentration, receptor occupancy and response. *J Clin Psychopharm* 33: 329–335.

Carnahan, R., Lund, B., Perry, P. and Chrischilles, E. (2006) Increased risk of extrapyramidal side-effect treatment associated with atypical antipsychotic polytherapy. *Acta Psychiat Scand* 113: 135–141.

Connolly, A. and Taylor, D. (2008) Ethnicity and quality of antipsychotic prescribing among in-patients in south London. *Br J Psychiat* 193: 161–162.

Connolly, A., Taylor, D., Sparshatt, A. and Cornelius, V. (2010) Antipsychotic prescribing in black and white hospitalised patients. *J Psychopharmacol*, 25: 704–709.

Constantine, R., Andel, R. and Tandon, R. (2010) Trends in adult antipsychotic polypharmacy: progress and challenges in Florida's Medicaid program. *Community Ment Health J* 46: 523–530.

Correll, C., Frederickson, A., Kane, J. and Manu, P. (2007) Does antipsychotic polypharmacy increase the risk for metabolic syndrome? *Schizophr Res* 89: 91–100.

Elie, D., Poirier, M., Chianetta, J., Durand, M., Grégoire, C. and Grignon, S. (2010) Cognitive effects of antipsychotic dosage and polypharmacy: a study with the BACS in patients with schizophrenia and schizoaffective disorder. *J Psychopharmacol* 24: 1037–1044.

Fenton, W., Blyler, C. and Heinssen, R. (1997) Determinants of medication compliance in schizophrenia: empirical and clinical findings. *Schizophrenia Bull* 23: 637–651.

Gee, S., Vergunst, F., Howes, O. and Taylor, D. (2013) Practitioner attitudes to clozapine initiation. *Acta Psychiat Scand* DOI: 10.1111/acps.12193.

Grech, P. and Taylor, D. (2012) Long-term antipsychotic polypharmacy: how does it start, why does it continue? *Ther Adv Psychopharmacol* 2: 5–11.

Harrington, M., Lelliott, P., Paton, C., Okocha, C., Duffett, R. and Sensky, T. (2002) The results of a multi-centre audit of the prescribing of antipsychotic drugs for in-patients in the UK. *Psychiatr Bull* 26: 414–418.

Haw, C. and Stubbs, J. (2003) Prescribing errors at a psychiatric hospital. *Pharm Pract* 13: 64–66.

Henderson, D., Fan, X., Copeland, P., Sharma, B., Borba, C., Boxill, R. *et al.* (2009) Aripiprazole added to overweight and obese olanzapine-treated schizophrenia patients. *J Clin Psychopharm* 29: 165–169.

Howes, O., Vergunst, F., Gee, S., McGuire, P., Kapur, S. and Taylor, D. (2012) Adherence to treatment guidelines in clinical practice: study of antipsychotic treatment prior to clozapine initiation. *Br J Psychiat* 201: 481–485.

Joukamaa, M., Heliövaara, M., Knekt, P., Aromaa, A., Raitasalo, R. and Lehtinen, V. (2006) Schizophrenia, neuroleptic medication and mortality. *Br J Psychiat* 188: 122–127.

Kane, J., Honigfeld, G., Singer, J. and Meltzer, H. (1988) Clozapine for the treatment-resistant schizophrenic: a double-blind comparison with chlorpromazine. *Arch Gen Psychiat* 45: 789–796.

Kapur, S. and Seeman, P. (2001) Does fast dissociation from the dopamine D2 receptor explain the action of atypical antipsychotics? A new hypothesis. *Am J Psychiat* 158: 360–369.

Kapur, S., Zipursky, R., Jones, C., Remington, G. and Houle, S. (2000) Relationship between dopamine D2 occupancy, clinical response and side effects: a double-blind PET study of first-episode schizophrenia. *Am J Psychiat* 157: 514–520.

Kuno, E. and Rothbard, A. (2002) Racial disparities in antipsychotic prescription patterns for patients with schizophrenia. *Am J Psychiat* 159: 567–572.

Leucht, S., Cipriani, A., Spineli, L., Mavridis, D., Örey, D., Richter, F and Davis, J. (2013) Comparative efficacy and tolerability of 15 antipsychotic drugs in schizophrenia: a multiple-treatments meta-analysis. *Lancet* 382: 951–962.

Lelliott, P., Paton, C., Harrington, M., Konsolaki, M., Sensky, T. and Okocha, C. (2002) The influence of patient variables on polypharmacy and combined high dose of antipsychotic drugs prescribed for in-patients. *Psychiatr Bull* 26: 411–414.

Lloyd, K. and Moodley, P. (1992) Psychotropic medication and ethnicity: an inpatient survey. *Soc Psych Psych Epid* 27: 95–101.

Mace, S. and Taylor, D. (2014) Reducing the rates of prescribing of antipsychotic high dose and polypharmacy on psychiatric inpatient and intensive care units: results of a 6-year quality improvement programme. *Ther Adv Psychopharmacology*.

NICE (2011) *Hypertension. Clinical management of primary hypertension in adults*. NICE Clinical Guideline 127. London: National Institute for Health and Clinical Excellance.

Nielsen, J., Dahm, M., Lublin, H. and Taylor, D. (2010) Psychiatrists' attitude towards and knowledge of clozapine treatment. *J Psychopharmacol* 24: 965–971.

Paton, C., Barnes, T., Cavanagh, M., Taylor, D. and Lelliott, P. (2008) High-dose and combination antipsychotic prescribing in acute adult wards in the UK: the challenges posed by p.r.n. prescribing. *Br J Psychiat* 192: 435–439.

Rummel-Kluge, C., Komossa, K., Schwarz, S., Hunger, H., Schmid, F., Lobos, C. and Leucht, S. (2010) Head-to-head comparisons of metabolic side effects of second generation antipsychotics in the treatment of schizophrenia: a systematic review and meta-analysis. *Schizophr Res* 123: 225–233.

Shi, L., Ascher-Svanum, H., Zhu, B., Faries, D., Montgomery, W. and Marder, S. (2007) Characteristics and use patterns of patients taking first-generation depot antipsychotics or oral antipsychotics for schizophrenia. *Psychiatr Serv* 58: 482–488.

Shim, J., Shin, J., Kelly, D., Jung, D., Seo, Y., Liu, K. and Conley, R. (2007) Adjunctive treatment with a dopamine partial agonist, aripiprazole, for antipsychotic-induced hyperprolactinemia: a placebo-controlled trial. *Am J Psychiat* 164: 1404–1410.

Taylor, D. (1997) Switching from typical to atypical antipsychotics. *CNS Drugs* 8: 285–292.

Taylor, D., Mir, S., Mace, S. and Whiskey, E. (2002) Co-prescribing of atypical and typical antipsychotics—prescribing sequence and documented outcome. *Psychiatr Bull* 26: 170–172.

Taylor, D., Paton, C. and Kapur, S. (ed.) (2012) *The Maudsley Prescribing Guidelines in Psychiatry*. Chichester: John Wiley and Sons.

Taylor, D. and Smith, L. (2009) Augmentation of clozapine with a second antipsychotic–a meta-analysis of randomized, placebo-controlled studies. *Acta Psychiat Scand* 119: 419–425

Thompson, A., Sullivan, S., Barley, M., Strange, S., Moore, L., Rogers, P. and Harrison, G. (2008) The DEBIT trial: an intervention to reduce antipsychotic polypharmacy prescribing in adult psychiatry wards–a cluster randomized controlled trial. *Psychol Med* 38: 705–715.

Van Dorn, R., Swanson, J., Elbogen, E. and Swartz, M. (2005) A comparison of stigmatizing attitudes toward persons with schizophrenia in four stakeholder groups: perceived likelihood of violence and desire for social distance. *Psychiatry* 68: 152–163.

Waddington, J., Youssef, H. and Kinsella, A. (1998) Mortality in schizophrenia. Antipsychotic polypharmacy and absence of adjunctive anticholinergics over the course of a 10-year prospective study. *Br J Psychiat* 173: 325–329.

Whiskey, E., Olofinjana, O. and Taylor, D. (2011) The importance of the recognition of benign ethnic neutropenia in black patients during treatment with clozapine: case reports and database study. *J Psychopharmacol* 25: 842–845.

Wyatt, R. (1991) Neuroleptics and the natural course of schizophrenia. *Schizophrenia Bull* 17: 325–351.

APPENDIX 16 CASE VIGNETTE

A 23-year-old, unemployed man presents to psychiatric services after being brought in by police having been found wandering in busy traffic.

He is somewhat agitated and confused and shows poor self-care. Since admission three days before, he says he has been hearing voices telling him to direct traffic and then discussing his inability to do this.

During interview he is markedly thought-disordered. On the ward he has been eating only takeaways, having told staff that he believes the hospital food to be poisoned. Nursing staff say that he has been isolating himself in his room during the day, coming out only when prompted to do so. There are no other mental state changes and he is taking no medication. The working diagnosis is of a relapse of schizophrenia.

He is a physically fit, white/black* man of average height and weight (about 75Kg) with no family history of mental illness. His mother and father are in good health as are his two siblings. He has had one other hospital admission. This was a year ago when he was treated with risperidone which he apparently stopped soon after discharge because of sexual side effects.

During this first admission he was assessed by a psychiatrist and diagnosed with schizophrenia. At that time he had been using cannabis heavily. However he claims he has not used any street drugs in the recent past – his urine drug screen confirms this. Alcohol use is moderate and he smokes 20 cigarettes a day.

Question

What antipsychotic medication(s) would you prescribe and at what dose?

Drug (s)	**Dose**	**Route**

*vignettes used white or black

APPENDIX 17 DEMOGRAPHIC DETAILS CASE VIGNETTE STUDY

Prescribing of Antipsychotics Survey

Demographic Details

Age		
Gender (please tick as appropriate)	**Male**	
	Female	
Grade (please tick as appropriate)	**Senior House Officer (Foundation Trainee)**	
	Speciality Registrar (Speciality Trainee)	
	Consultant	
Ethnicity (please tick as appropriate, from Office of National Statistics census classifications)	**White**	
	Mixed/Multiple ethnic groups	
	Black/African/Caribbean/black British	
	Asian or Asian British	
	Other ethnic group	

Pharmacy Department
Maudsley Hospital
Denmark Hill
London
SE5 8AZ

Maudsley Hospital
Denmark Hill
London
SE5 8AZ

1st July 2014

Dear

Survey of Antipsychotic Prescribing

I am undertaking a brief survey of psychiatrists' prescribing of antipsychotics. I am afraid I cannot give further details of the aims of the survey without running the risk of influencing responses.

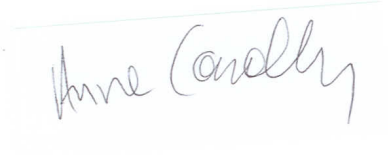
I can tell you that the survey has not been funded by the pharmaceutical industry but is part of an approved PhD programme.

The survey should take **no longer than five minutes** to complete and asks only one question. Please return by email or, if anonymity is desired, please send it back to me in the internal post.

I will keep a record of the responders (that are not anonymous) and send them a report of the survey when complete.

Thank you in advance for your time and opinions.

Yours sincerely



Anne Connolly
Principal Pharmacist, South London and Maudsley NHS Trust

APPENDIX 19 IS MY STUDY RESEARCH?

Go straight to content.

NHS
Health Research Authority

MRC Medical Research Council

Is my study research?

To print your result with title and IRAS Project ID please enter your details below:

Title of your research:

attitudes of medical professionals to prescribing by race

IRAS Project ID (if available):

You selected:

- **'Yes'** - Are the participants in your study randomised to different groups?
- **'No'** - Are any treatments allocated by randomisation?
- **'No'** - Does your study protocol demand changing treatment/ patient care from accepted standards for any of the patients involved?
- **'No'** - Are your findings going to be generalisable?

Your study would NOT be considered Research by the NHS.

You may still need other approvals.

Researchers requiring further advice (e.g. those not confident with the outcome of this tool) should contact their R&D office or sponsor in the first instance, or the **HRA** to discuss your study. If contacting the HRA for advice, do this by sending an outline of the project (maximum one page), summarising its purpose, methodology, type of participant and planned location as well as a copy of this results page and a summary of the aspects of the decision(s) that you need further advice on to the HRA Queries Line at **HRA.Queries@nhs.net**.

For more information please visit the **Defining Research** leaflet

Follow this link to start again.

Print This Page

APPENDIX 20 CASE VIGNETTE STUDY

Therapeutic Advances in Psychopharmacology *Original Research*

Does race affect prescribing for acute psychosis? Evaluation by a case vignette

Ther Adv Psychopharmacol
1–6
DOI: 10.1177/2045125316638051

Anne Connolly and David Taylor

Abstract

Background: Black people are over represented in mental health services and prescribing of antipsychotics differs by race in some countries. Our previous UK research into the prescribing of antipsychotics in large, multicentre studies found no important differences for black and white patients. However, we received several comments challenging our findings. We wanted to test the validity of these anecdotes by devising two case vignettes that differed only by race and asking prescribers to choose antipsychotic treatment.

Method: A case study was sent to all medical prescribers in the South London and Maudsley NHS Trust. Half of the prescribers for each grade of staff were sent the case study where the ethnicity of the patient was white and the other half where the ethnicity was black. Participants were asked to describe what they would prescribe for the patient. Outcomes were total percentage maximum dose, high dose, type of antipsychotic, route of administration and antipsychotic polypharmacy.

Results: We received 123 completed case studies and demographic data forms from prescribers. There were no differences in percentage maximum dose, high dose, type, route and number of antipsychotics prescribed by case study ethnicity.

Conclusions: Prescribing for UK black and white patients is broadly similar when tested in clinical and theoretical studies.

Keywords: antipsychotic agents; ethnic groups; psychotic disorders

Introduction

Black people are over represented in mental health services [Care Quality Commission, 2010] and they are more likely to be admitted and detained than their white counterparts [Morgan *et al.* 2006; Care Quality Commission, 2010]. In addition, deaths of black service users [Norfolk, Suffolk and Cambridgeshire Strategic Health Authority, 2003] have resulted in accusations of institutional racism in UK mental health services [McKenzie and Bhui, 2007]. The implication is that this racism is reflected in different prescribing practices for black people.

Prescribing of antipsychotics differs by race in some countries. Studies, mostly in the United States, show black patients are more likely to receive higher doses, typical antipsychotic agents and greater numbers of antipsychotics than white patients [Diaz and De Leon, 2002; Kreyenbuhl *et al.* 2003; Taylor, 2004]. However, several UK studies have not shown major differences in prescribing quality between black and white patients [Connolly *et al.* 2007, 2011; Connolly and Taylor, 2008]. Previously we examined dose, type, polypharmacy and costs of antipsychotics in large, multicentre studies. There were no important differences between treatments for black and white patients. Possible reasons for this difference in findings from US studies include a more equitable healthcare system in the UK, a diverse multicultural mental health workforce [Goldacre *et al.* 2004] and changing attitudes to racism.

After publication of our studies examining antipsychotic prescribing in black and white patients, we received several comments challenging our findings. Black and minority ethnic group prescribers reported disbelief at our results. They claimed that black patients have a longer duration

Correspondence to:
Anne Connolly, BPharm, MRPharmS
Pharmacy Department, Maudsley Hospital, London SE5 8AZ, UK
anne.connolly@slam.nhs.uk

David Taylor, BSc, MSc, PhD FRPharmS FFRPS
Pharmacy Department, Maudsley Hospital, London, UK

of untreated psychosis (a suggestion disproved in the UK by the AESOP study [Morgan *et al.* 2006]) and a greater illness severity (a potentially confounding factor not accounted for in our previous study) on admission [Arnold *et al.* 2004]. Because of these differences, prescribers told us, they purposefully prescribed larger doses for black patients.

We wanted to test the validity of these anecdotes in a formal way in a wider population of prescribers at one centre from our original study [Connolly *et al.* 2011]. We did this by devising two case vignettes that differed only by race and asking prescribers to choose antipsychotic treatment(s) and dose(s).

Method

A case study (see Appendix 1), demographic data form (collecting age, gender, grade of staff and prescriber ethnicity) and explanatory letter were sent to all medical prescribers in the South London and Maudsley NHS Trust. Half of the prescribers for each grade of staff were sent the case study where the ethnicity of the patient was white and the other half where the ethnicity was black. Respondents could reply by email or anonymously in the post. Prescribers who did not respond were sent a reminder email after 2 weeks.

The case study asked two questions: what antipsychotic(s) would you prescribe for this patient and what dose(s) would you use? The explanatory letter asked prescribers to complete a survey of antipsychotic prescribing. It stated that the reasons for the study could not be revealed as they would invalidate the results. The case study was piloted before distribution to ensure it was fit for purpose and could be easily completed. Study permission was obtained from the South London and Maudsley NHS Trust Drugs and Therapeutics Committee.

Statistical analysis

The outcomes analysed were: total percentage maximum dose (calculated as dose divided by maximum British National Formulary (BNF) dose [BMJ Group and Pharmaceutical Press, 2014], multiplied by 100); high dose (more than 100% of BNF maximum dose); type of antipsychotic (typical or atypical); route of administration (oral or intramuscular); and antipsychotic polypharmacy (being prescribed more than one antipsychotic). Descriptive statistics were calculated for prescribers' demographic data and inferential statistics were used for each outcome by case ethnicity. In addition relationships between outcomes and prescriber demographic data were explored using inferential statistics, i.e. *t*-test and analysis of variance (ANOVA) for continuous and chi-squared for categorical outcomes. Continuous variables were transformed when lacking normality and categorized where appropriate to ease interpretation. All analyses were performed using IBM SPSS software.

Results

Study population

We sent 784 case vignettes and demographic data forms to prescribers. Of these, 123 (15.7%) were completed and returned. Clinical and demographic characteristics of prescribers are detailed in Table 1. The mean age of the prescribers (n = 115) was 39.1 years (range 25–63). A total of 63 (51.2%) of the returned case vignettes were those where the patient was described as white.

Outcomes

Descriptive data for each of the categorical outcomes (high dose, type, polypharmacy and route) are listed in Table 2.

Total dose (percentage maximum dose). There was no significant difference in total dose of antipsychotic by case ethnicity (p = 0.567) (see Table 3). The mean total doses for black and white patients were 47.7% and 50.9%, respectively (Figure 1).

Type of antipsychotic. Aripiprazole then olanzapine were the most frequently chosen antipsychotics accounting for 82.1% of choices (Figure 2). Prescribers often gave several possible treatment options in reply to the case vignette questions, for example, olanzapine or aripiprazole or quetiapine or risperidone. These were labelled in the order written as antipsychotic 1 or antipsychotic 2 or antipsychotic 3 or antipsychotic 4. There was no difference by case vignette ethnicity in type (typical or atypical) of antipsychotic 1 (Figure 3), antipsychotic 2, antipsychotic 3 or antipsychotic 4.

Antipsychotic polypharmacy, high dose, route of administration outcomes. There were no differences

Table 1. Categorical clinical and demographic characteristics of prescribers.

Demographic	Category	Frequency $n = 123$ (%)	Missing
Gender	Male	76 (61.8%)	0
Grade	Consultant	50 (41%)	1
	Specialist trainee	42 (34.4)	
	Core trainee	12 (9.8)	
	Foundation trainee	18 (14.8)	
Ethnicity	White	88 (72.7)	2
	Asian	18 (14.9)	
	Black	8 (6.6)	
	Mixed	4 (3.3)	
	Other	2 (1.7)	
	Chinese	1 (0.8)	

Table 2. Categorical outcomes of case vignette.

Outcome	Category	Frequency $n = 123$ (%)	Missing
Type of antipsychotic 1*	Atypical	117 (95.1)	0
	Typical	5 (4.1)	
	Not an antipsychotic	1 (0.8)	
Type of antipsychotic 2*	Atypical	23 (18.7)	0
	Typical	3 (2.4)	
	Not an antipsychotic	2 (1.6)	
	None	95 (77.2)	
Type of antipsychotic 3*	Atypical	12 (9.8)	0
	Typical	1 (0.8)	
	None	110 (89.4)	
Type of antipsychotic 4*	Atypical	1 (0.8)	0
	Typical	0	
	None	122 (99.2)	
Polypharmacy (more than 1 antipsychotic prescribed)	Yes	12 (9.8)	0
High dose (more than 100% BNF maximum)	Yes	6 (5)	3
Route	Oral	111 (90.2)	0
	IM	1 (0.8)	
	Oral or IM	11 (8.9)	

*As explained in Results.
BNF, British National Formulary.

Table 3. Total dose and case ethnicity.

Total dose (% maximum)	Case ethnicity	*n*	Mean percentage maximum	Significance (two-tailed)
Antipsychotic 1	Black	60	41.82	0.632
	White	63	43.46	
Antipsychotic 2	Black	11	53.31	0.846
	White	15	51.10	
Antipsychotic 3	Black	4	62.50	0.101
	White	8	38.78	

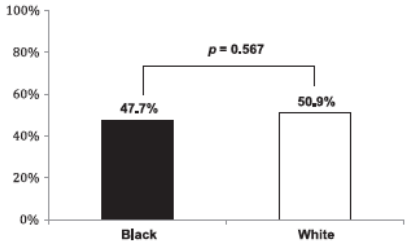


Figure 1. Total dose (percentage maximum) by case ethnicity.#

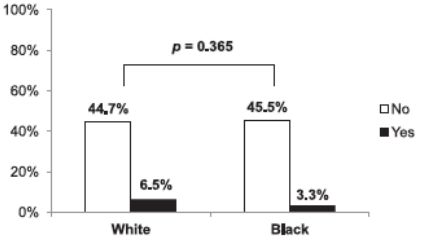


Figure 4. Polypharmacy (more than one antipsychotic prescribed) by case ethnicity.

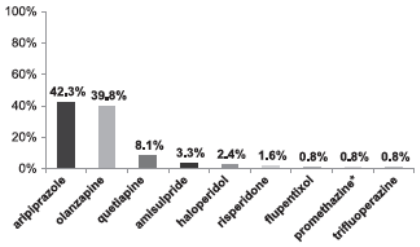


Figure 2. Choice of antipsychotic by case ethnicity.
#First antipsychotic listed as explained in Results.
*Not an antipsychotic.

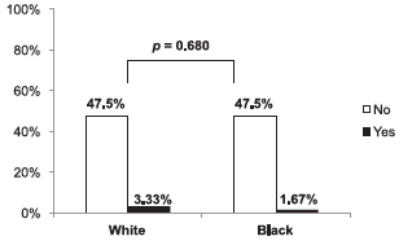


Figure 5. High-dose antipsychotic (more than 100% BNF maximum dose) by case ethnicity.
BNF, British National Formulary

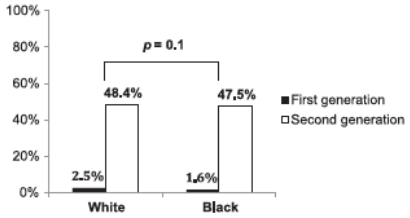


Figure 3. Type of antipsychotic by case ethnicity.

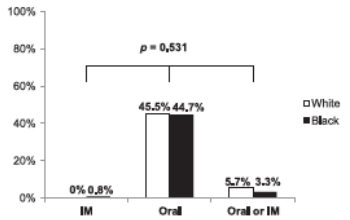


Figure 6. Route of antipsychotic by case ethnicity.
IM, intramuscular.

in antipsychotic polypharmacy ($p = 0.365$, Figure 4), high dose prescribing ($p = 0.680$, Figure 5) and route of administration ($p = 0.531$, Figure 6) by case ethnicity.

Prescriber variables and outcomes

Each prescriber variable (age, gender, grade of staff and ethnicity) was examined to determine whether associated with our outcomes (total dose, high dose, polypharmacy, type and route).

Total dose. Age was not normally distributed but three discreet categories were evident. These three categories were: 32 years old or less, 33–44 years old and 45 years old or more. Mid-aged (33–44 year olds) prescribers were more likely to use higher doses ($p = 0.01$). Gender, grade of staff and prescriber ethnicity were not significantly associated with total dose.

High dose. As with total dose, mid-aged prescribers were more likely to prescribe high doses

($p = 0.04$). Gender, grade and prescriber ethnicity were not significantly associated with high dose.

Polypharmacy. Mid-aged prescribers were more likely to prescribe more than one antipsychotic concurrently ($p = 0.001$). Gender, grade and prescriber ethnicity were not significantly associated with polypharmacy.

Type and route. We found no association between any prescriber variables for type and route outcomes.

Discussion

Main findings

We found no difference in antipsychotic prescribing by ethnicity when examined using a case vignette method. This included analysis of total dose, high dose, polypharmacy, type and route of antipsychotics chosen. In addition prescriber variables, with one exception, were not associated with any of our outcomes.

Comparison with previous studies

A similar method to that used in this study has been used previously to test differences by race in the treatment of patients with mental health problems. The study of British psychiatrists [Lewis *et al.* 1990] used a case vignette, differing by race (black or white) and gender, to determine effects of these variables on treatment. Interestingly they found that psychiatrists rated white patients as significantly more likely than black to need 'neuroleptic treatment'. In addition to this they also found no differences by race in 'antidepressant treatment not indicated' and 'unlikely to comply'. This study was revisited in 2001 by Minnis and colleagues [Minnis *et al.* 2001]. Again they used a case vignette but also attached a photograph of a white or black man. Similarly, these later authors also found that white patients were more likely than black to have 'neuroleptic drug treatment indicated'. Thus, as in this study, prior case-based questionnaires did not find black patients were more likely to receive antipsychotics.

Limitations

We had a poor questionnaire return rate compared with previous studies. This may be because the vignettes were emailed and so could be easily ignored as prescribers receive large volumes of unsolicited email. A reminder was sent out, again by email, and did improve response rates.

Poor return rates may also have been because prescribers guessed the reasons for our study. Other studies [Lewis *et al.* 1990; Minnis *et al.* 2001] did not ask for prescribers' ethnicity directly as we did. This was because they were concerned that this would unmask their studies. Instead they collected indirect indicators of ethnicity, i.e. medical school of graduation; however, some of their respondents still guessed correctly. We cannot be sure if any of our prescribers knew, or whether or not some were suspicious. No prescribers we spoke to guessed correctly the purpose of the study, but many were concerned that the case vignette was for a 'prescribing test' set by our Trust and that there were 'correct answers'.

Conclusion

Our original conclusions about antipsychotic prescribing quality and ethnicity are supported by the results of this study. Prescribing for UK black and white patients is broadly similar when tested in clinical and theoretical studies. In this and previous studies we have found no adverse bias in prescribing practice related to ethnicity.

Acknowledgements

The authors of this article wish to thank Olubanke Dzahini for her statistical support and advice.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of interest statement

The authors declare no conflicts of interest in preparing this article.

References

Arnold, L., Strakowski, S., Schwiers, M., Amicone, J., Fleck, D., Corey, K. *et al.* (2004) Sex, ethnicity, and antipsychotic medication use in patients with psychosis. *Schizophr Res* 66: 169–175.

BMJ Group and Pharmaceutical Press (2014) *British National Formulary 68th Edition*. London: BMJ Group and Pharmaceutical Press.

Care Quality Commission (2010) *Count me in 2010: results of the 2010 national census of inpatients in mental health and learning disability services in England and Wales*. London: Care Quality Commission.

Connolly, A., Rogers, P. and Taylor, D. (2007) Antipsychotic prescribing quality and ethnicity: a study of hospitalized patients in south east London. *J Psychopharmacol* 21: 191–197.

Connolly, A. and Taylor, D. (2008) Ethnicity and quality of antipsychotic prescribing among in-patients in south London. *Br J Psychiat* 193: 161–162.

Connolly, A., Taylor, D., Sparshatt, A. and Cornelius, V. (2011) Antipsychotic prescribing in black and white hospitalised patients. *J Psychopharmacol* 25: 704–709.

Diaz, F. and De Leon, J. (2002) Excessive antipsychotic dosing in 2 U.S. state hospitals. *J Clin Psychiatry* 63: 998–1003.

Goldacre, M., Davidson, J. and Lambert, T. (2004) Country of training and ethnic origin of UK doctors: database and survey studies. *Br Med J* 329: 597.

Kreyenbuhl, J., Zito, J., Buchanan, R., Soeken, K. and Lehman, A. (2003) Racial disparity in the pharmacological management of schizophrenia. *Schizophr Bull* 29: 183–193.

Lewis, G., Croft-Jeffreys, C. and David, A. (1990) Are British psychiatrists racist? *Br J Psychiat* 157: 410–415.

McKenzie, K. and Bhui, K. (2007) Institutional racism in mental health care. *Br Med J* 334: 649–650.

Minnis, H., McMillan, A., Gillies, M. and Smith, S. (2001) Racial stereotyping: survey of psychiatrists in the United Kingdom. *Br Med J* 323: 905–906.

Morgan, C., Dazzan, P., Morgan, K., Jones, P., Harrison, G., Leff, J. *et al.* (2006) First episode psychosis and ethnicity: initial findings from the AESOP study. *World Psychiat* 5: 40–46.

Norfolk, Suffolk and Cambridgeshire Strategic Health Authority (2003) Independent inquiry into the death of David Bennett. Cambridge, UK: Norfolk, Suffolk and Cambridgeshire Strategic Health Authority.

Taylor, D. (2004) Prescribing of clozapine and olanzapine: doseage, polypharmacy and patient ethnicity. *Psychiat Bull* 28: 241–243.

Appendix 1

Case vignette

A 23-year-old, unemployed man presents to psychiatric services after being brought in by police having been found wandering in busy traffic.

He is somewhat agitated and confused, and shows poor self-care. Since admission 3 days before, he says he has been hearing voices telling him to direct traffic and then discussing his inability to do this.

During interview he is markedly thought disordered. On the ward he has been eating only takeaways, having told staff that he believes the hospital food to be poisoned. Nursing staff say that he has been isolating himself in his room during the day, coming out only when prompted to do so. There are no other mental state changes and he is taking no medication. The working diagnosis is of a relapse of schizophrenia.

He is a physically fit, white/black [vignettes used white or black] man of average height and weight (about 75 kg) with no family history of mental illness. His mother and father are in good health as are his two siblings. He has had one other hospital admission. This was a year ago when he was treated with risperidone, which he apparently stopped soon after discharge because of sexual side effects.

During this first admission he was assessed by a psychiatrist and diagnosed with schizophrenia. At that time he had been using cannabis heavily. However, he claims he has not used any street drugs in the recent past – his urine drug screen confirms this. Alcohol use is moderate and he smokes 20 cigarettes a day.

Question

What antipsychotic medication(s) would you prescribe and at what dose?

Drug (s)	Dose	Route